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Postgraduate Medicine

VOLUME I, Number 1

JANUARY 1947

Special articles in this issue

TREATMENT OF BRAIN INJURIES

by **Dr. Alfred W. Adson**, PROFESSOR OF
NEUROSURGERY, UNIVERSITY OF MINNESOTA,
GRADUATE SCHOOL OF MEDICINE, ROCHESTER,
MINNESOTA

ORGANIC VARIABILITY IN HEART DISEASE

by **Dr. William F. Petersen**, DIRECTOR
OF CLINICAL RESEARCH, ST. LUKE'S HOSPITAL, CHICAGO

**Some of the Common ERRORS in the TREATMENT of
FRACTURES of the EXTREMITIES**

by **Dr. James J. Callahan**, ASSOCIATE
PROFESSOR OF BONE AND JOINT SURGERY, LOYOLA
UNIVERSITY SCHOOL OF MEDICINE

TREATMENT OF ACNE

by **Dr. Earl D. Osborne**, PROFESSOR
AND HEAD OF THE DEPARTMENT OF DERMATOLOGY,
UNIVERSITY OF BUFFALO SCHOOL OF MEDICINE

Diagnostic Clinics

DISEASES OF THE THYROID

by **Dr. George Crile, Jr.**,
CLEVELAND, OHIO

TREATMENT OF SYPHILIS

by **Dr. Harold N. C.**
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JANUARY, 1947

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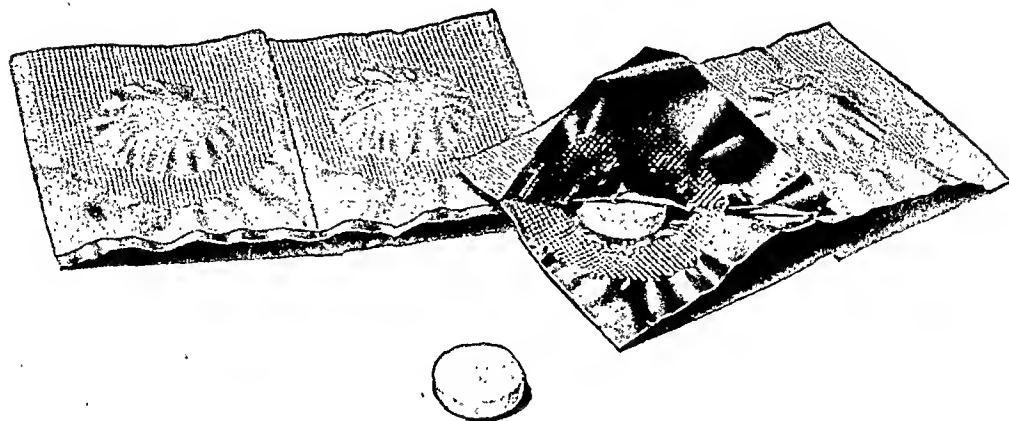
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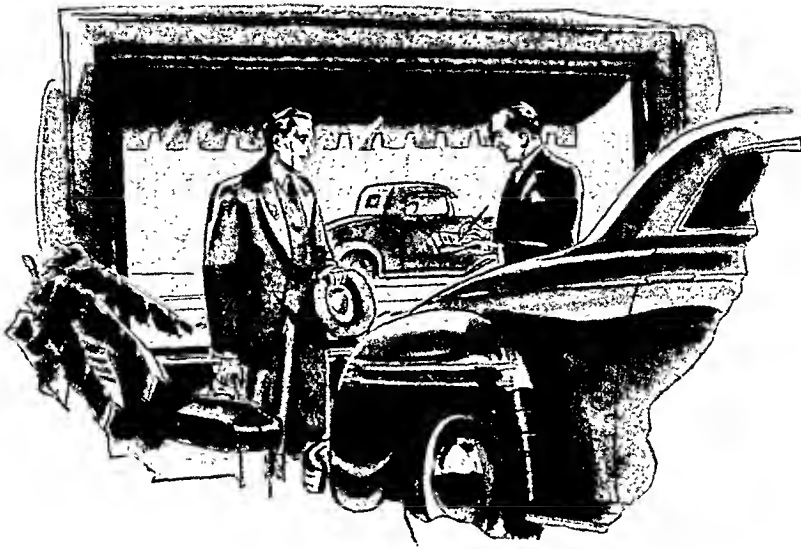


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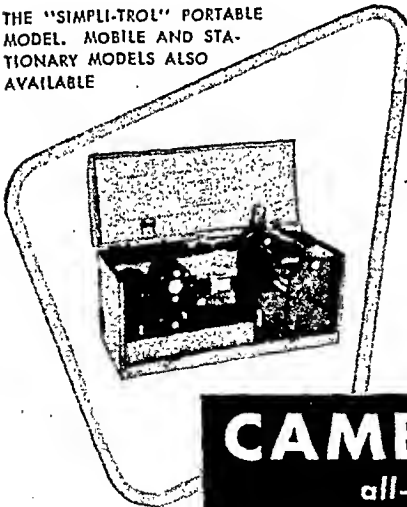


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Fig. 1. Die and counter die method of forming plate. From Baker, G. S.: Cranioplasty with tantalum plate: a new method of forming the plate prior to operation. Proc. Staff Meet., Mayo Clin. 21:177-182 (May 1) 1946.

fluid waves as the result of the impact may also be an explanation for the temporary unconsciousness. According to Munro, a violent histologic insult to the brain must be predicated to produce such changes.

CEREBRAL COMPRESSION differs from concussion in that the state of unconsciousness is prolonged and is due to increased intracranial pressure of cerebral laceration. The disturbance of consciousness may vary from a short period of semiconsciousness, a dazed or confused state, to one of deep coma. Many of the patients are restless and delirious. The majority regain consciousness within hours to three or four days, while in others the loss of consciousness may continue for several weeks.

Treatment of shock—Though it may be difficult to distinguish between the symptoms that are due to general shock and those due to cerebral shock, the emergency treatments are very similar. Heat should be applied in the form of warm blankets; skeletal fractures should be temporarily supported; stimulants such as caffeine and ephedrine should be administered. In the event of severe hemorrhages, the foot of the bed may be raised and a transfusion administered. As soon as the blood pressure returns to

normal and the body becomes warm, examinations should be conducted.

A general examination to determine the extent of bodily injuries other than that to the head should be conducted in conjunction with a neurologic examination. The neurologic examination may be rather unsatisfactory in a comatose or non-cooperative patient, but it is possible to determine whether or not one or both pupils are dilated or whether a squint is present. It is also possible to determine whether or not a flaccid or a rigid paralysis exists and whether the reflexes are normal, lost or exaggerated, or if localized ecchymosis or hemorrhage from the ear or from the nasal orifices is present. The appearance of cerebrospinal fluid from the ear or nasal passages or from the compound fracture is significant. Roentgenographic examinations of the head in the anteroposterior and lateral views and roentgenographic examinations of suspected fractures of other bones are of inestimable value.

When immediate surgical intervention is indicated, it may become necessary on admission to the hospital to take the patient to the operating room, where reparative procedures

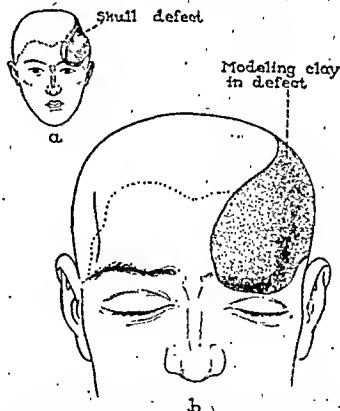


Fig. 2. Filling-in defect with modeling clay; first stage of method. From Baker, G. S.: Cranioplasty with tantalum plate: a new method of forming the plate prior to operation. Proc. Staff Meet., Mayo Clin. 21:177-182 (May 1) 1946.

can be employed simultaneously with the treatment of shock and other bodily injuries. In the event that the patient is delirious a sedative is necessary, but one should never administer morphine since it is a respiratory depressant. The barbiturates, sodium iso-amylethyl barbituric acid and pentobarbital sodium, are the most effective. If it becomes necessary to anesthetize the patient during the emergency surgical procedures, a general anesthetic may be necessary, for a delirious patient rarely cooperates with the surgeon even though the latter anesthetizes the scalp with a local anesthetic. The anesthetic that has proved of greatest value is sodium ethyl thiobarbiturate administered intravenously.

IN CLEANSING and repairing a scalp, skull and brain wound, care should be taken to shave hair well beyond the wound, remove all foreign material, trim the traumatized edges, remove spicules of bone and prolapsed brain, and aspirate cerebral clots. An aqueous solution of mercurial germicide is used for cleansing and for washing the wound. In the case of compound comminuted fractures of

On the completion of the emergency surgical treatment of the head injury and other bodily injuries, the patient is returned to his bed, where the treatment for shock is continued. The administration of antitetanic and antigas serum is indicated when abrasions, cuts or lacerated wounds have been sustained. It should not be given until the patient has recovered from general shock. Oftentimes it is wise to delay the injection of these serums until the day following the injury.

Fractures—Fractures of the skull may be divided into three groups: linear, depressed and comminuted, all of which may or may not be compound.

The linear fractures most frequently involve the base of the skull and fairly frequently extend into the nasal sinuses or across the temporal bone. The hemorrhages accompanying them are not serious unless the tears in the meninges extend across meningeal arteries or the cavernous sinus. Linear fractures across the temporal bone frequently result in tearing of the middle meningeal artery with the development of an extradural hemorrhage. Linear fractures extending across the longitudinal or lateral sinuses may have an accompanying tear in the venous sinuses with the development of both an extradural and a subdural hemorrhage. The basal fractures which result in tearing of the meninges will manifest themselves by localized ecchymosis and the escape of blood-tinged cerebrospinal fluid from the nose or the ear. Accumulations of blood will produce signs of increased intracranial pressure.

Injuries to the oculomotor nerves will be evidenced by oculomotor palsies; injuries of the petrous portion of the temporal bone are usually associated with facial paralysis and deafness. The symptoms resulting from extradural hemorrhages are delayed, and it is fairly common for a patient to regain consciousness for several hours following the injury and then to lapse again into a state of coma. Extradural hemorrhages also produce a unilateral dilatation of the pupil and a contralateral spastic hemiplegia. Therefore, a patient should be kept under close observation for the first forty-eight hours when-

ever a fracture is situated over a meningeal artery or a large sinus. Accumulation of blood in the posterior fossa or trauma to the cerebellum produces nystagmus and cerebellar ataxia and occasional paralysis of the sixth nerve. Fractures of the floor of the posterior fossa may result in tears of the ninth, tenth, eleventh and twelfth cranial nerves.

DEPRESSED fractures vary in extent and location. Small depressed fractures over the silent regions of the brain may be of no serious consequence and need no surgical treatment just as simple linear fractures need no special treatment. If, however, the depressed fracture tears an important vessel the blood clot will need to be evacuated and the hemorrhage controlled. If a depressed fracture occurs in the frontal bone an elevation is indicated for cosmetic reasons. The elevation of such a fracture may be postponed until the patient has recovered from the immediate effects of his head injury. Depressed fractures over the motor, speech or visual centers should be elevated as soon as the traumatic shock has been treated.

Comminuted fractures may or may not be depressed. Whenever the physical examination or the roentgenographic examination reveals spicules driven into the brain they should be withdrawn and the fragments should be elevated, replaced and held in position by silver wire ties if the wound is not compound. Most depressed fractures are comminuted; occasionally it is possible, after making a single trephine opening, to introduce an elevator under the depression and restore its former contour. In the event that fragments of bone are removed, plastic repair may be performed at some later date. Occasionally if the bony defect is small, no repair is necessary unless the fracture has occurred in the frontal bone, when, for cosmetic reasons, a repair is indicated.

Control of hemorrhages—Extradural arterial hemorrhages are controlled through a decompression type of craniotomy or through a small flap craniotomy by the application of a silver clip, by ligation of the vessel with silk or by the electrocoagulating needle. Extradural clots

are evacuated and the pockets are cleansed with saline solution. If a marked cerebral depression has resulted, a small tube drain should be left in place for twenty-four hours. Tears in the large sinuses should be explored at the location of the fracture across the sinus. This is done by trephining over the location and enlarging it

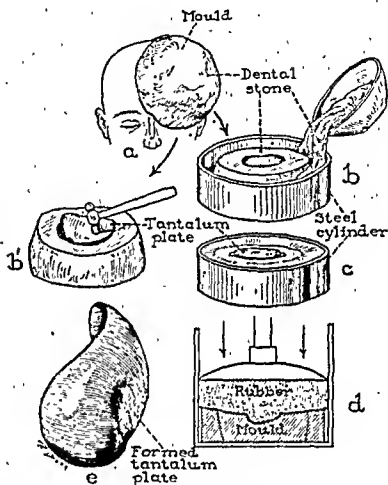


Fig. 3a to e. Method of forming mold and the plate. From Baker, G. S.: Cranioplasty with tantalum plates: a new method of forming the plate prior to operation. *Proc. Staff Meet., Mayo Clin.* 21:177-182 (May 1) 1946.

sufficiently to expose the tear. Rents in the sinus are repaired by the application of a pledget of muscle which is held in place by a wick of gauze for seventy-two hours. The dura, lateral to the sinus, should be incised in order to determine whether or not the tear in the sinus has resulted in an extravasation of venous blood into the subdural spaces. Such lacerations are also repaired by pledgets of muscle. The subdural hemorrhages are removed by repeated aspirations and saline washings. The dura is closed with either catgut or silk, depending on whether or not the wound is compound.

Occasionally subdural hemorrhages result

from tears in small vessels extending from the dura to the arachnoid. These tears result in slow extravasations of blood with the development of symptoms of intracranial pressure or focal signs of compression. These injuries may not be accompanied by skull injury. The suspicion of a subdural hematoma justifies burr-hole openings and incisions in the dura to clarify the diagnosis. Occasionally a patient will appear to recover from the symptoms of an acute head injury, but fail to regain his normal health. Drowsiness may persist; headaches may continue; focal signs may fail to disappear weeks or even months after a head injury. When this occurs one must consider the possibility of a subdural hematoma. A diagnostic encephalogram may reveal distorted contours in the ventricular system and a failure in the equal distribution of air in the subarachnoid spaces. Since the subdural hemorrhage is free to travel between the dura and the arachnoid on both sides of the brain, it is wise to trephine on both sides to avoid overlooking the subdural hematoma on the contralateral side of the injury. Subdural hematomas, unless they have been of long duration, can be aspirated and the pockets washed with saline solution by the employment of a small catheter which is attached to a syringe. If the hemorrhage has been extensive it may be necessary to make two or three trephine openings and leave a No. 18 catheter as a through-and-through drainage to prevent any subsequent refilling of the cavities. The brain will eventually expand by the refilling of the ventricles and the subarachnoid spaces. This may be hastened by forcing the amount of liquids taken by the patient.

HEMORRHAGES of the base from tears in the dura are not easy to cope with. If one is in doubt, a temporal exploratory decompression is indicated. With an illuminated retractor it is possible to elevate a cerebral lobe and control the meningeal bleeding with an electrocoagulating needle. Hemorrhages from a cerebral vessel can be controlled in a similar manner or with the aid of a silver clip. Usually the hemorrhages are not severe unless a branch of the meningeal

artery is torn or the cavernous sinus has been injured. The latter injury, when it occurs, results in such a rapid extravasation of blood that the patient frequently succumbs before surgical treatment can be instituted. If one is fortunate enough to localize the hemorrhage from a vein of the cavernous sinus it is controlled with a pledget of muscle by a technic similar to that employed when injuries occur to the superior longitudinal and lateral sinuses.

As a rule, it is not wise to attempt a repair of the meninges when an escape of cerebrospinal fluid occurs from the nasal sinuses or the middle ear. One should not perform spinal punctures or spinal drainage for fear of reversing the current and drawing nasal discharges into the meningeal spaces. The judicious use of sulfonamides serves as a prophylactic measure in minimizing the development of meningitis. The introduction of sterile cotton pledgets into the external ear serves as another protective measure. Usually the cerebrospinal fluid ceases to drip within a week or ten days. Should a cerebrospinal fistula develop, an intracranial repair of the meninges by suture or by the application of a muscle pledget should not be undertaken within less than eight to twelve weeks following the head injury.

Tears in the meninges, especially in the region of the ethmoid and frontal sinus, result not only in cerebrospinal leaks, but occasionally in pneumo-encephalos. These can be visualized by roentgenographic examination. Most of them disappear spontaneously, but occasionally an air cavity may exist for weeks. If it is of any serious size a trephine opening may be employed for the introduction of a brain cannula and the withdrawal of the air in the cavity.

Hygromas—Hygromas may simulate subdural hematomas in symptomatology since a tear in the arachnoid which usually occurs along the sylvian fissure permits cerebrospinal fluid to enter the space between the dura and the arachnoid where it becomes locked. These are corrected by performing a small decompression, opening the dura and allowing the fluid to escape. Again a small tube drain is left in place for several days until the ventricles

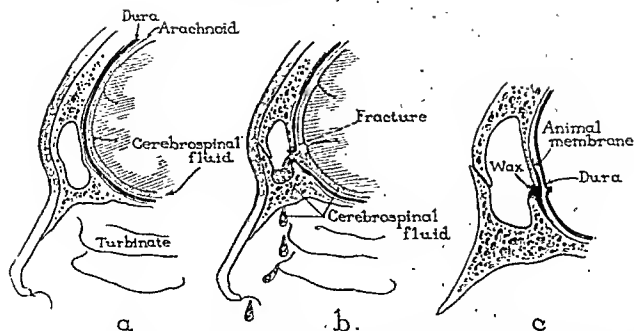


Fig. 4a. Normal relationships of the brain, meninges and skull in the frontal region; b, cranius fistula with leakage of cerebrospinal fluid into the frontal sinus and thence into the nose; c, plastic closure of the meninges and occlusion of the bony defect with wax. From Adson, A. W.: Cerebrospinal rhinorrhea: surgical repair of cranius fistula. *Ann. Surg.* 114:697-705 (Oct.) 1941.

expand and force the brain against the dura and the cranial wall.

Cerebral trauma—Cerebral trauma varies from a localized bruise with punctate hemorrhages to extensive lacerations of the brain. The *contrecoup* injuries may be as great as those at the point of impact. The skull injury is rarely an indication of the extent of the cerebral injury. The degree of coma, the state of the pulse, respirations, blood pressure, and the evidence of neurologic signs furnish the only accurate evaluation of the cerebral injury. Even then it may be difficult to arrive at an accurate opinion, since a rapidly developing cerebral edema or intracranial hemorrhage may exaggerate the symptoms. If symptoms of a localized condition exist, an exploratory decompression may be required to eliminate the possibility of an intracranial hemorrhage. The symptoms resulting from cerebral edema are more or less diffuse; restlessness or coma may persist for hours or days without evidence of localized paralysis.

Intracranial pressure—Increased intracranial pressure usually follows a craniocerebral injury.^{14, 16} It results from cerebral edema and intracranial hemorrhages. With the absence of

localizing signs one is justified in performing a spinal puncture. The reading of the spinal pressure indicates the degree of intracranial pressure. Spinal drainage may prove effective in controlling the intracranial pressure. On the other hand, if the spinal pressure is not particularly increased, the pulse is not slowed and the respirations are not stertorous, one need not be greatly alarmed and the so-called do-nothing treatment may be the advisable course to follow.

HOWEVER, if signs of increasing intracranial pressure appear, the course of dehydration should be followed. It consists of employing limitation of fluids to 1,000 cc. for the first twenty-four hours and the administration of magnesium sulfate by enema, dissolving 2 ounces (62 gm.) of salts in 4 fluid ounces (118 cc.) of water, to be followed by intravenous administration of 50 cc. of 50 per cent solution of glucose or sucrose. Unfortunately the effects of intravenous administration last for only four to six hours. A repetition of the intravenous administration may be required during the first forty-eight hours. After the first twenty-four hours, I prefer to administer glucose in 20 per cent solution in quantities of 500 cc. repeated twice or three times daily.

THE DEHYDRATION measures are supplemented by repeated spinal drainage if the two procedures give evidence of controlling the intracranial pressure, but it should be remembered that if the initial treatment of the cerebral edema by dehydration and spinal drainage is ineffective a large temporal decompression, or even a suboccipital decompression, should be resorted to. Though some surgeons prefer the decompression method for the control of cerebral edema, I prefer to give the dehydration and spinal drainage as a therapeutic test before resorting to surgical intervention, and I have also found that the dehydration may even supplement the effects of a decompression.

If the patient has not regained consciousness by the third day, one should be rather cautious about extending the dehydration too far, since the patient automatically dehydrates himself by the loss of fluid through respiration, perspiration and excretion. As a rule, we introduce a Rehfuß tube into the stomach by way of the nasal passages in order to administer 2,000 cc. of water and nourishment, and saline cathartics if we think it necessary to continue a moderate degree of dehydration. From the third day until the patient becomes conscious, fluid and nourishment are administered through this tube in small quantities at hourly intervals.

The problem of controlling restlessness is very perplexing at times. I dislike the use of morphine, since it is a respiratory depressant. Codeine is rarely effective; the barbiturates are the most useful. Phenobarbital in rather large doses, $1\frac{1}{2}$ grains (0.1 gm.) every six hours, is usually sufficient. In the more violent cases, sodium iso-amylethyl barbiturate or pentobarbital sodium is required. I dislike to restrain a patient and believe that it is less injurious to the patient to be narcotized by the more potent barbiturates than to be forcibly restrained by wrist and leg bands. In a few instances it has been necessary to administer sodium ethyl thio-barbiturate intravenously as an initial sedative.

CONVALESCENT TREATMENT

On the return of consciousness the physician too often concludes that the patient has recov-

ered from his cerebral injury, but it should be remembered that if the patient is dismissed from hospital care before he has thoroughly recovered, he will complain of headache, weakness, dizziness and nervousness, will become discouraged and will develop a series of fear complexes. Therefore, whether the patient remains in the hospital or returns to his home he should be kept under supervision and directed concerning his activities, his diet and rehabilitative measures. A patient who has sustained a serious craniocerebral injury should not be permitted to return to his regular work for from four to eight weeks. He should be encouraged to rest and sleep several hours during the day, be allowed to sit up for only short periods at a time at the onset, take graduated exercises, and eat a well-balanced diet with limitation of fluids to 2,000 or 3,000 cc. per day. Saline cathartics may be required to regulate his intestinal habits for the first two weeks, following which he can depend on the proper selection of foods, including fruits, for the re-establishment of his intestinal habits. If palsies have developed, physical therapy should be administered. Frequent assurances should be given in order that the patient may regain confidence in himself.

In the event that irreparable damage has resulted from the craniocerebral injury, it becomes the duty of the attending surgeon to aid the patient in selecting a change of vocation and insurance adjustment, for if the surgeon is negligent in aiding the patient to rehabilitate himself the latter may become a permanent invalid instead of a useful or partly useful individual.

POSTTRAUMATIC SEQUELAE

The most common type of posttraumatic sequela is that of headache, dizziness and fear of being unable to work, losing one's job and not receiving adequate compensation for one's injury. The headache and dizziness may continue off and on for six months to two years. These two symptoms may result from a low-grade communicating hydrocephalus due to a failure to absorb the cerebrospinal fluid. The failure to absorb the cerebrospinal fluid probably is due to subarachnoid hemorrhage, low-

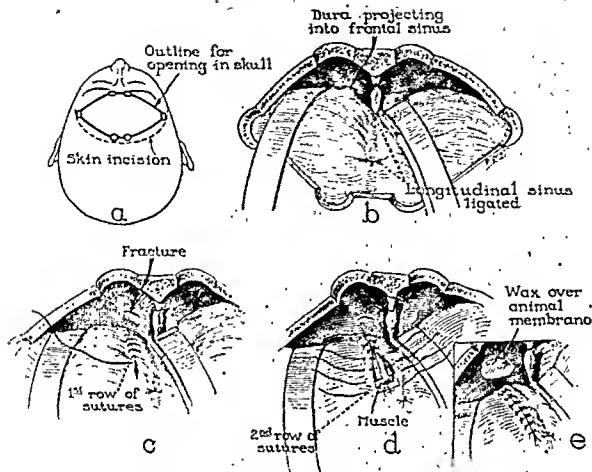


Fig. 5a. Schematic outline of incision in the scalp and craniotomy.

Fig. 5b. Elevation of dura, identification of the fistulous tract and ligation of the longitudinal sinus.

Fig. 5c. Closure of the dural tear with a suture of continuous catgut.

Fig. 5d. Re-enforcement of the primary closure by means of a second row of interrupted silk sutures, including a strip of muscle employed as additional protection against recurrence of the rhinorrhea.

Fig. 5e. Closure of bony opening with animal membrane and bone wax. From Adson, A. W.: *Corebrospinal rhinorrhea: surgical repair of cranius sinus fistula*. *Ann. Surg.* 114:697-705 (Oct.) 1941.

grade leptomenigitis and a fibrosis of certain stomas in the pachionian bodies. The final adjustment of secretion and absorption results when an automatic balance between the two takes place. Limitation of fluids to 1,800 cc. a day and the occasional administration of a saline cathartic appear to give some relief from headache and dizziness. Sedatives occasionally are resorted to, but usually acetylsalicylic acid is sufficient. The economic fears are eliminated by not forcing the patient to return to work before he is able and by making sure that he is capable of fulfilling the tasks assigned to him and that a fair compensation has been made, either by the insurance company or by the industrial labor commission.

Epilepsy—Epilepsy occurs in about 5 per cent of craniocerebral injuries. It occurs most fre-

quently when the frontotemporoparietal regions have been traumatized. Convulsions may occur at the time of injury or may appear weeks, months or years subsequently, and the extent of the injury is not always an indication as to whether or not epilepsy will develop. Occasionally convulsive seizures may be eliminated on the resection of the focal scars or the evacuation of traumatic cysts, but more often than not surgical procedures for the treatment of post-traumatic epilepsy are disappointing. The medical treatment consists of medication, the use of sedatives such as phenobarbital, bromides, dilantin and tridione. A medical regimen of dehydration and the use of a ketogenic diet have offered assistance in the treatment of epilepsy.

Posttraumatic psychosis—Posttraumatic psy-

chosis, though not common, does occur. In a few instances it is temporary; however, evidence of cerebral deterioration persists though the manic symptoms may subside.

*Cerebral abscess*²—Suppurative head wounds and cerebral abscesses have been greatly reduced in frequency with the introduction of débridement procedures and the ample use of the sulfonamides and penicillin. Sulfanilamide may be used in wounds where brain tissue has been lacerated, but this cannot be said of sulfathiazole. Penicillin may be applied directly to a craniocerebral wound. A solution of the same may be used to irrigate a lacerated wound of the brain. Although local application of sulfanilamide and penicillin is effective in reducing incidence of suppuration, administration of sulfanilamide by mouth and of penicillin by intramuscular or intravenous injections is much more effective. Administration should be continued for one week as a prophylactic measure to prevent cerebral abscess when missiles or fragments of scalp or bone have been driven into the brain. Symptoms of a developing cerebral abscess may not appear for ten to twenty days following the injury. The most suitable time to drain such abscesses is when encapsulation of the abscess has taken place. This can be recognized by an approach of the septic type of temperature curve to normal and a fall of the leukocyte count. The abscess should be drained at the point of cerebral injury. Adequate and thorough drainage should be instituted in two to three weeks from the onset of the abscess. The drainage tube should be left in place for another two or three weeks, the tube being shortened as the cavity closes and granulates from the bottom.

Skull defects—Skull defects resulting from the removal of fragments of bone in a compound comminuted fracture of the skull do not always need plastic closures when they are small or are located over postcentral areas of the brain. However, if they are extensive or are located in the frontal area, a plastic closure is indicated even though it may only be for cosmetic reasons.

Our war experiences have shown that tanta-

lum plate is the metal of choice, since it is inert and malleable. I should like to quote from my colleague, Dr. George S. Baker, who has had an extensive war experience with the use of tantalum in closing defects in the skull.

"A tantalum plate can be easily made at the operating table⁴ when the defect is not complicated. The defects difficult to repair are those that occur in the frontal bone with involvement of the frontal sinuses. In these cases the cosmetic result is of paramount importance. Few special instruments are necessary for making the plate at the table and these can be sterilized with others that are necessary to complete the operation. The size of the defect is measured by a piece of sterile lead foil or cottonoid. The tantalum plate is then cut with scissors from the pattern. It is easily shaped by hammering over a concave metal mold until it assumes the contour of the removed bone.

"When the operation is a secondary one, it is perhaps best to mold the plate prior to operation by the die and counter die method (Fig. 1)¹¹ or by the direct method (Figs. 2 and 3).⁴ The scalp is cleanly shaved and in each case an identical mold of the defect is obtained, allowing one-quarter to one-half inch (0.6 to 1.3 cm.) extension beyond the edge of the bone. The plate is cut to proper size. Either it is hammered into shape on the mold or a power press is used to swage the metal. The latter method is recommended when a press is available. The thickness of the temporal muscle must always be accommodated for making plates in the temporal region. Small holes can be made in the plate with a Crutchfield brace and dental burr, or a metal punch. When the finished plate is sterilized it is ready for insertion.

TECHNIC OF CRANIOPLASTY WITH TANTALUM PLATE

"The scalp is cleanly shaved and prepared for operation as in craniotomy. Local anesthesia is recommended in most cases, but complicated repairs are best handled while the patient is under general anesthesia or a combination of the two. Attempts should be made to resect scars of the scalp when secondary procedures

are being done. The primary repairs are completed through the original exposure, but in secondary operations it may be necessary to make a new incision for adequate blood supply to the flap and for better exposure of the defect. Once the area has been satisfactorily exposed two methods of insertion of the plate are in use to complete the cranioplasty; namely, the onlay method and the inlay method described by Hemberger, Whitcomb and Woodhall.¹² The secondary repairs often require injection of solution of penicillin (10,000 units per cubic centimeter) under the plate or scalp flap as prophylaxis against reinfection. Fibrin foam that has been saturated with penicillin and thrombin has been used to good advantage by the author in such cases when control of hemostasis was difficult in old scar tissue and a concentration of penicillin was desirable for bacteriostasis to safeguard against infection.

"Compression dressings of sponge latex or mechanic's waste are advisable to prevent accumulation of fluid beneath the flap. When fluid appears it should be removed by aspiration and a compression dressing should be reapplied. The tissues of the scalp soon become adherent to the tantalum plate and it is a very rare occasion when the plate has to be removed because of foreign body reaction.

CONCLUSIONS

"The cosmetic appearance of patients who have submitted to cranioplasty has been unusually gratifying. The physiologic effect of covering the defect of the skull in posttraumatic cases has invariably improved the symptoms of vertigo and headache. The psychologic advantage to the patient has been a notable accomplishment."

CEREBROSPINAL RHINORRHEA

Causation—Cerebrospinal rhinorrhea⁴ may result from a number of causes, the most common of which is skull fracture that extends through the posterior wall of the frontal sinus (Figs. 4a and b) or the cribriform plate of the ethmoid bone, with accompanying tears of the

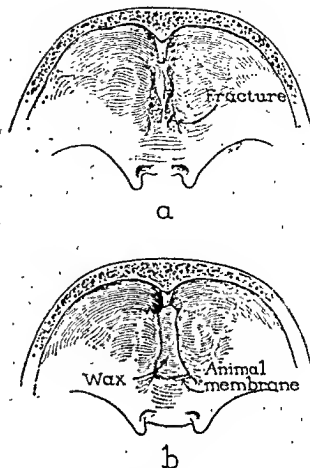


Fig. 6a. Fracture of the cribriform plate; b, closure of the bony defect with animal membrane and bone wax. From Adson, A. W.: Cerebrospinal rhinorrhea: surgical repair of craniosinus fistula. *Ann. Surg.* 114:697-705 (Oct.) 1941.

dura and arachnoid.^{5, 10} The first evidence of rhinorrhea associated with fracture of the skull is the occurrence of a watery, bloody discharge from the nose. In most instances, in my experience, the lesions heal with spontaneous remission of the rhinorrhea. Persistent rhinorrhea or the delayed occurrence of rhinorrhea usually is due to considerable loss of bone, absorption of a fragment of bone or inclusion of the dura and arachnoid between fragments of bone, which permits escape of cerebrospinal fluid into one of the nasal cavities.

CEREBROSPINAL rhinorrhea frequently has occurred spontaneously. When it does occur, it probably is the result of a congenital defect in the cribriform plate which permits extension of an envelope of arachnoid along an olfactory nerve fiber through the cribriform plate. Leakage of cerebrospinal fluid undoubtedly is the result of rupture of the thinned-out arachnoid

and mucous membrane. According to reviews in the literature, precipitation of this type of rhinorrhea usually is the result of coughing or sneezing during an attack of head cold. Rhinorrhea has accompanied hydrocephalus, and in that particular instance leakage of cerebrospinal fluid was the result of increased intracranial pressure on thinned-out membranes and absorptive defects of the cribriform plate. I have also seen the condition afflict two patients suffering from pituitary tumor. The floor of the sella turcica had been absorbed, with presumable leakage of cerebrospinal fluid into the sphenoidal sinus. I also saw the condition when a large osteoma of the orbit had extended through the ethmoid into the anterior fossa.

RHINORRHEA also has followed removal of nasal polyps. The polyps probably were meningoceles that had extended through the cribriform plate. Rhinorrhea also has resulted from craniotomy when, in the making of the anterior margin of the bone flap, the frontal sinus was unintentionally opened.

Symptoms and signs—The only symptom that many patients complain of is an annoying, watery discharge of the nose. It may be continuous or cease for only a few hours before it recurs. The discharge may appear as drops of clear fluid or it may pour out in a stream when the head is tilted in certain positions. Usually, it appears in one side of the nose and produces the sensation that is experienced when the nose is congested. In acute injuries of the head, it may be difficult to recognize cerebrospinal fluid because it is mixed with blood, but when the condition is chronic the fluid is watery and can be readily collected and examined chemically. Cerebrospinal fluid is colorless, limpid, slightly viscous, has a specific gravity of 1.004 to 1.008, and contains traces of protein and small quantities of inorganic salt and dextrose. The lymphocyte count varies from 5 to 10 cells per cubic centimeter of fluid.

If there is doubt about the presence of cerebrospinal fluid in a discharge from the nose, the indigo carmine test, in which 1 cc. of indigo

carmine is introduced into the subarachnoid space of the spinal canal by means of routine spinal puncture, might be employed. Since the dye promptly stains the cerebrospinal fluid, a bluish green color will be seen to appear in the nasal discharge within about fifteen minutes and will continue for two or three hours, if fluid discharging from the nose contains cerebrospinal fluid. This test is of particular value in the differentiation between cerebrospinal rhinorrhea and allergic and vascular rhinorrhea. Roentgenologic examination of the skull offers some aid in the diagnosis in cases of recent fracture, but rarely is such examination of much assistance in the localization of cerebrospinal fistula involving the ethmoid cell.

Meningitis is the serious complication which may result from cerebrospinal rhinorrhea. It occurs more often when rhinorrhea results from fracture of the skull than it does when rhinorrhea occurs spontaneously, but it is a constant threat in all cases, and especially so when the patient has contracted a nasopharyngeal infection. Fortunately, chemotherapy has proved of value in combating meningitis and also has made it possible to perform the extensive operations for closure of craniosinial fistulas without fear of the development of meningitis.

Conservative treatment—Conservative treatment (nonoperative) often has been employed by those who feared to advise or employ the radical procedure designed to close the fistulous tract. The argument set forth by those who advocate conservative treatment is that they believe it safer not to disturb the patient than it would be to hazard a radical operation. Unfortunately, there is little to offer in the way of nonoperative treatment.

Surgical treatment—The accepted procedures for closure of craniosinial fistulas which communicate with the frontal sinus, the ethmoid cells or the nasal cavity have been: (1) in cases in which the condition is acute, surgical repair through the frontal sinus; (2) in cases in which the condition is chronic and it is possible to identify the site of the lesion, performance of small unilateral transfrontal craniotomy, identification of the fistula and closure of the

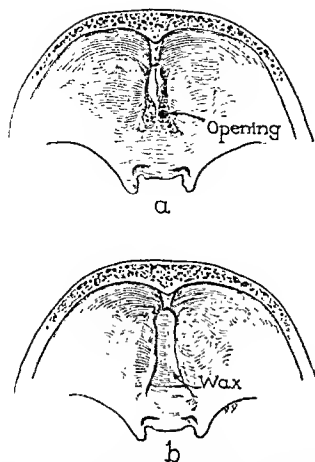


Fig. 7a. Congenital defect of the ethmoid bone; b, closure of the bony defect with wax. From Adson, A. W.: Cerebrospinal rhinorrhea; surgical repair of craniocsinus fistula. *Ann. Surg.* 114:697-705 (Oct.) 1941.

meningeal opening with interrupted silk sutures or closure of it with sutures and covering of it with muscle; or (3) performance of unilateral transfrontal craniotomy, in which the dura is elevated, the opening is identified and a wick of iodoform gauze is placed between the lacerated dura and the cribriform plate, as Peet has advocated. The end of the gauze wick is brought out through the frontal incision but the wick itself is left in place for four days and then carefully removed. Peet¹³ stated, "The object of this procedure is to prevent meningitis by allowing the brain to become firmly adherent to the lacerated dura, thereby effectively closing off the subarachnoid space before organisms passing through from the nose can cause infection."

I have used these accepted procedures with varied success; the one difficulty that I always have encountered in attempting to free the dura from the cribriform plate is that the dura has had a tendency to tear, as Grant emphasized in his discussion of Coleman's paper. The dura, in addition to being thin, is likewise under

moderate tension, preventing the carrying out of proper overlapping of the dura which is necessary for thorough invagination of the meningeal fistulous tract. I have included muscle in the suture line to assure against leakage of cerebrospinal fluid. I have further attempted to assure against recurrence of rhinorrhea by filling the bony defect with Horsley's bone wax (Fig. 4c), but in spite of all these precautions, recurrence of rhinorrhea has occurred. This failure prompted development of the operation employed in these cases of chronic rhinorrhea, in which cure has been obtained.

THE PROCEDURE consists of performance of craniotomy which will allow the dura to be elevated from the bone in both halves of the frontal fossa. The bone flap must be designed so as to extend across the midline and to uncover the anterior poles of both frontal lobes (Fig. 5a). A coronal scalp-flap incision is employed. It is placed within the hairline, after which the scalp and periosteum are reflected forward to a line just above the frontal sinus. Six trephine openings are made, the first two of which are placed on each side of the midline just above the frontal sinus. The second two trephine openings are placed on each side of the midline and the longitudinal sinus, approximately 3 cm. in front of the coronal suture. The third two openings are placed in the temporo-frontal region, one on each side. As the bone between all the openings is cut with a Gigli saw, an opening is effected which is sufficient to permit elevation of the dura and the frontal lobes. The bone flap is kept sterile during the operation by means of a sponge soaked with saline solution.

Caution is taken to avoid injury to the longitudinal sinus. Bleeding from the longitudinal sinus is controlled by ligation of the sinus (Fig. 5b) with silk ligatures at a level 6 cm. above the foramen cecum, which is situated superior to the crista galli. In some instances, it is necessary to ligate the longitudinal sinus where it communicates with the foramen cecum. The advantage of ligation of the longitudinal sinus is that it allows the dura to be sutured into, and,

if necessary, to be used in closure of the fistulous tract. The procedure is continued by elevation of the dura from the frontal fossa and the olfactory grooves, where it is necessary to sacrifice the olfactory nerves. The elevation of the dura is continued until the anterior crest of the sella turcica is approached. During this dissection, the fistulous tract is always encountered, whether it be situated on the right or the left side. The meninges will be seen to extend into the defect of the frontal sinus or the cribriform plate.

After the dura has been mobilized sufficiently and the fistulous tract has been identified, plastic closure of the tract is begun by overlapping of the dura in such a way as to invaginate the meningeal portion of the fistula. The first suture is placed in the most dependent part of the elevated dura (Fig. 5c). The suture is No. 0 continuous chromic catgut. The primary line of suture is protected by a strip of muscle which is transfixed to the dura and further reinforced by the placing of a second row of interrupted silk sutures (Fig. 5d). The defect in the frontal sinus or cribriform plate is filled with Horsley's bone wax. Further to protect against forcing of the wax through the cranial defect into the sinus or nose, Lukens' animal membrane is placed over the defect before the introduction of wax to plug the hole (Figs. 5e, 6 and 7).

The advantages of bifrontal craniotomy are: (1) A better exposure is obtained than by employment of a unifrontal flap; (2) the surgeon is always sure to identify the fistulous tract; (3) the exposure thus obtained affords a better opportunity for elevation of the meninges along the cribriform plate; and (4) after elevation of the dura from the cribriform plate, tension on the dura is relieved; this permits greater ease of invagination of the fistulous tract and successful performance of overlapping dural closure of meningeal defects. The postoperative appearance of one patient who had a congenital defect in the ethmoid bone is shown in Fig. 8.

BEFORE replacement of the bone flap, thorough hemostasis should be effected. A rubber tissue drain can be used but is not neces-



Fig. 8. Postoperative appearance of the patient who had the congenital defect in the ethmoid bone. From Adson, A. W.: Cerebrospinal rhinorrhea: surgical repair of cranio-sinus fistula. *Ann. Surg.* 114:697-705 (Oct.) 1941.

sary because no cerebrospinal fluid will be seen to escape. The bone flap is wired in place with noncorrosive wire, inserted through perforations which are placed opposite each other in the skull and bone flap. The periosteum, galea and scalp are closed with interrupted silk sutures.

As a precautionary measure, administration of sulfanilamide is continued for three days prior to operation until the concentration of sulfanilamide in the blood reaches a value of from 8 to 12 mg. per 100 cc. Likewise, it is continued for ten days after operation, during which time the same concentration of the drug in the blood is maintained. The dosage that I have employed ranged from 45 grains (3 gm.) to 90 grains (6 gm.) per day. In no instance did meningitis develop during the postoperative period.

Fractures of the skull extending into the base and involving the middle fossa result fairly frequently in tears of the blood vessels within the area and give rise to aneurysms and arterio-

venous fistulas between the intracranial portion of the internal carotid artery and the cavernous sinus. The treatment is designed to close the tear by inserting plugs of muscle into the internal carotid artery or to trap the fistulous opening by ligating the internal carotid artery in the neck and also ligating it within the cranium on the cerebral side of the aneurysm or the arteriovenous fistula. However, it should be borne

in mind that no attempt at ligation should be done until it has been ascertained that a ligation can be performed without producing contralateral hemiparesis. This is accomplished by employing the Matas procedure, which consists in compressing the common carotid artery from a few minutes to thirty minutes three times a day without producing any untoward effects or paresis.

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Treatment of Acne

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ACNE, the commonest disease process known to man, is a disease that requires the attention of every man in general practice and a great many men in the specialties. It is a disease that probably caused more man-hours lost during the war than almost any other condition, because complications of acne were foremost in all the theatres of the war where excessive heat, moisture and healthy young men were present. Acne, although it may sound like a simple thing, and it may be to some of you, is an exceedingly important subject from the standpoint of general care, man-hours lost in the war and the development of neuroses in young women and young men. Furthermore, it is a disease for which something can be done if we will but understand the basic process involved.

The incidence of the disease, I do not need to tell you, is exceedingly high. It is estimated by competent authorities that at least 50 per cent of young people between the ages of 17 and 25 manifest some degree of acne vulgaris. Personally I think that estimate is a little too low.

I shall not spend much time on the symptomatology of the disease because you are all acquainted with it and have all seen cases of acne. I merely want to call your attention to

some of the more important features of the disease. Acne always begins as a dilatation of the duct of the sebaceous gland, a formation of a plug through hyperkeratosis of that duct, the backing up of secretion, the deposit of oily or lipoid substances, a secondary inflammatory reaction, the development of pustules, followed by discharge and scarring if the lesion is deep enough.

One of the complications of a later stage of acne is the rosacea type that comes in middle age. I shall have something to say regarding the treatment of this disfiguring condition. This used to be much more common than it is today, but we still quite frequently see patients with marked rhinophyma. The principal process in the development of rhinophyma is first the basis of acne, the development of rosacea, the cystic enlargement of the sebaceous glands of the skin of the nose, followed by the laying down of fibrous tissue from chronic inflammatory reaction. Treatment of this sort of condition is extremely satisfactory today.

The basis of severe rosacea with rhinophyma is always acne. Sebaceous follicles are dilated. Before appearance of a bulbous nose severe acne vulgaris with scarring and pitting occurs and the entire skin of cheeks, nose, forehead, chin and neck are filled with pits at the site of the old lesions of acne vulgaris.

Deep nodular lesions may develop and remain for many months before pustulation takes place, before there is sufficient inflammatory

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reaction to produce abscess. These lesions then break down and discharge to the outside, leaving pitted scars which are first red and after six months to a year become white. Many old lesions remain three, four and even five years. Obviously the patient experiences great mental disturbance and many young women go into hiding for periods of three, four, five, six, or ten years.

Typical in a young man with the same condition are comedones, commonly called blackheads, large cystic lesions, scarring and cystic lesions on the forehead.

If one understands the histogenesis of acne vulgaris, handling of the case becomes clear. There is a marked inflammatory reaction to lipid substances with the presence of bacteria. First there is plugging of the duct; the secretion backs up; comedones form in the duct and the outer margin of the comedone turns black. You call it a blackhead, but actually that blackness is due to the oxidizing effect on the sulfides in the sebaceous secretion and the cells lining the duct. The color is not due to dirt or lack of washing the face.

Sooner or later, infection, which is always present, develops in the dammed-up secretion with the cellular elements. There is perforation of the membrane of the secreting gland, allowing lipid substances to pass into the surrounding tissue and setting up a lipid foreign-body reaction with secondary phagocytosis, inflammatory reaction, and the formation of an abscess. If the patient or doctor squeezes the lesion at this point, infection is squeezed out into the normal tissues to each side and a furuncle or a carbuncle is likely to form.

The rosacea type on the faces of individuals 45 to 50 or 55 years of age is made up more of a red papular element with more vascular dilatation around the lesion, giving rise to the telangiectasia or new capillary formation in the skin. There is usually less of the pustular element in rosacea.

IN TREATING patients for acne vulgaris the doctor should always remember that the normal course of the disease is one of quiescence

and exacerbation. If one follows a group of, say, 100 patients with acne vulgaris over a period of three years without treatment, he will find that approximately 20 to 25 per cent clear up entirely in that time without any treatment; approximately 40 per cent more will be free of the disease half the time and will show active lesions the rest of the time and the remaining 35 per cent will show continuous acne with flare-ups and quiescences.

The etiology of the disease is also of great importance in the treatment. It is possible to have the patient show comedones at any age. We have seen comedones in babies a year and a half and two years of age. This undoubtedly is due to a disturbance in the balance of endocrine function. We know very little about it. It is unquestionably a premature endocrine stimulation of the sebaceous glands of the skin.

Heredity is an important factor in all acne-form conditions—the seborrheic state, let us say. One inherits a skin which is blessed with a larger or lesser number of sebaceous glands; one also inherits a background of endocrine activity, and it is usual to note in an entire family of father and mother and several children that where one or both of the parents have acne, several of the children have it, and where acne is not present in the parents, few of the children have acne.

The next consideration regarding etiology is the presence of the acne bacillus. One can almost always demonstrate the acne bacillus in the lesions of acne vulgaris; that is, anywhere from the comedones through the nodules, papules, pustules, abscesses. That does not prove that the acne bacillus is the pathogenic agent. It is believed now by most observers that staphylococci are the principal secondary invaders. In a very high proportion of patients exhibiting acne lesions it is possible to grow staphylococci from the ducts of the sebaceous glands. They are nearly always present below the plug which forms in the duct, so that if conditions are right in the sebaceous gland, there is bound to be secondary infection sooner or later, with the formation of abscesses.

It was believed for some time by numerous



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observers that focal infection was important in the etiology of acne vulgaris and related states. Most observers at the present time, including myself, are of the opinion that it has no influence whatever that cannot be explained on an endocrine basis, because the endocrine balance is affected by all infections. I merely want to state that focal infection per se has nothing to do directly with the etiology of the disease. The same is true of intercurrent infections. It has been noted repeatedly that individuals suffering from intercurrent infections in the hospital are apt to develop an exacerbation of acne. Again, that is all explainable on an endocrine basis.

I want to say quite a few words regarding the nutritional factor in the etiology of acne. We have been through a great many years of observation, research and guessing in the use of diets in treating acne vulgaris. Fortunately I have gone through all of those periods. It is not sufficient to put ten or fifteen patients on a particular type of diet for three to six months and at the end of that time evaluate those cases and say, "Well, 50 per cent of them are better and therefore the credit belongs to that diet."

That is merely the normal course of the disorder.

Thirty or more years ago and right up to within fairly recent times, ten or fifteen years ago, it was thought that a high carbohydrate diet was the principal factor in inducing acne vulgaris. In the past fifteen years there have been quite a number of series of patients put on high carbohydrate diets, patients with and without acne, to see the effect. Furthermore; quite a number of series of patients with acne vulgaris have been put on exceedingly low carbohydrate diets to note the effect. The consensus of most competent observers is that the amount of carbohydrates in the diet has no influence on the course of acne vulgaris.

I might dismiss the protein factor. No one has ever been able to demonstrate that there has been a protein factor in the causation of acne.

WITHIN the last eight to ten years there have been a number of observations suggesting that a hyperlipemia with high fat diet was a definite factor in the production of acne, and in one of our most recent and honored textbooks on dermatology there is quite a treatise on fats or hyperlipemia as a definite factor in the cause of acne. There are many qualified men in this country today who believe that. I happen to be one of those individuals, however, who do not entirely agree with that stand, and for this reason: We took a series of 50 patients with acne and placed them on a very low fat diet. We saw no difference at all in the outcome from any of our others. Then we took 50 patients who had acne vulgaris and fed them high fat diets, and again we were unable to say there was any appreciable effect. Our next observation covered a series of patients with severe acne vulgaris, the worst cases having large nodular lesions, deep abscesses and cysts. We took very careful histories of their dietary régime as far back as the patient and the relatives could go, and we were unable to demonstrate that these patients ingested a high fat diet. As a matter of fact, from our experience we concluded that, if anything,

these patients with the severest acne had a low fat intake. So we are a bit skeptical that the high fat diet is much of a factor in the production of acne. I shall have more to say about that in a moment.

Next I want to speak about the glandular factor. It is well known from scientific observation that injections of the male sex hormone testosterone will induce acne. Furthermore, we know that eunuchs do not have acne. We also know from observation that a fairly high percentage of females with acne have a definite exacerbation of the acne at the menstrual period or the period of ovulation, two or three days prior to the menstrual period. That occurs in about 50 to 60 per cent of young females having acne.

There have been a great many observations along this line into which I shall not go, but I do want to say definitely that we have enough scientific evidence at the present time to indicate that an endocrine imbalance is the factor behind the production of acne vulgaris and is the primary factor.

There may be many secondary factors and a high fat diet inducing a hyperlipemia may enter into the picture. I want to emphasize, however, that an endocrine imbalance is the background of acne vulgaris, and it is possible to develop acne vulgaris with that endocrine imbalance without any evidence of a high fat diet. It is possible to have severe acne with an endocrine imbalance with an exceedingly low carbohydrate diet, and it is possible to have a severe acne without the patient's eating large quantities of chocolate, which has been incriminated.

WE NEED more scientific observations in acne vulgaris before we jump at erroneous conclusions regarding food factors, but we now are certain that the endocrines have a great bearing on the problem.

There are a few other observations of importance that have been generally made, two of them along the same line. One is that constant blood-letting causes acne to disappear. It has been observed in groups of donors in emer-

gencies where they have given large donations of blood that acne disappears. Some of the diet enthusiasts have stated that was due to reducing the hyperlipemia or the hyperglycemia. Actually, competent observers think it suggests a removal of excess quantities of hormonal substances.

I want to devote the few remaining moments to a discussion of treatment. In the first place, I want to eliminate some of the erroneous impressions that have been abroad in the last twenty years. One is regarding the value of vaccines. That, of course, has been exploded in our literature. Vaccines are of no value in acne vulgaris. Furthermore, staphylococcus toxoids are of no value.

I have already discussed the nutritional factor, and I might say that I am not at all against the use of a low fat diet as advised by many individuals. It does no harm, but from a purely scientific standpoint I cannot rely on that for results.

All estrogenic substances have proved failures under scientific observation. There have been enthusiasts who have reported original benefit. The injection of pregnancy urine has produced remarkable results in a rather high percentage of individuals in the age group of 17 to 25, and of course that brings up the question of antuitrin-S. The use of antuitrin-S in young people up to the age of 23 to 25 will have a definite beneficial effect in about 50 to 60 per cent of those individuals. The injections have to be given two or three times a week, and in sufficient dosage to produce a result, but the trouble with the treatment is that as soon as you stop it the acne returns. Therefore, it is a poor form of treatment and I believe most competent men have given it up.

The use of thyroid is definitely indicated in all cases of acne vulgaris. We know from careful observation of large series of patients with acne receiving no other treatment, that at least 50 per cent of the young group between the ages of puberty and 23 to 25 are benefited by thyroid medication. We usually start with $\frac{1}{2}$ grain of the extract or double that amount of desiccated thyroid. In individuals who are ob-

viously hypothyroids we gradually increase the dose to one grain a day, watching the symptomatology at all times. We have found that it is of no value to take routine basal metabolic rates.

Ingestion of bromides and iodides should be discontinued. Bromides and iodides are follicular irritants and will cause any acne to become worse as well as start an acne in an individual otherwise free. That includes iodized salt.

Constipation is not a factor in acne and has nothing to do with it.

FINALLY, as to the use of surgery and x-ray, I am against the constant surgical opening and expression of all the comedones and small pustules which may be present. I would advise careful opening with a small sharp knife and curettage of any of the large cystic lesions. In our experience it is not necessary to be continually removing comedones and small pustules. It frequently produces more scarring than less.

There is no question at all that at the present time x-ray is still a necessary and exceedingly valuable adjunct in the treatment of acne vulgaris. It must be given by an experienced,

trained individual, preferably by one who knows dermatology. I do not advise the system of weekly treatments of a set dosage for a certain number of treatments. Every patient should be individualized and treated accordingly.

To those of you who are interested in x-ray, let me say that for the average case of acne the kilovoltage should not exceed 70. You want soft rays that will not penetrate more than 2 mm. For individuals who have cystic lesions, you must use a harder type of ray, preferably one with 70 kilovolts, using 1 mm. of aluminum filtration.

The treatment should be carried on at a very safe dosage and for a safe period of time. Reliance, however, on x-ray alone to cure patients with acne vulgaris is a mistake.

In addition to the use of x-ray we might mention local applications. Any method that will cause the skin to peel is good treatment, whether it be sunlight, lotio alba or any other solution. I particularly want to recommend for local use one of the newer preparations, intradermal sulphur, advocated by Dr. George M. MacKee of New York City. It consists of a penetrating sulphur compound put up in a penetrating vehicle, and it assists materially in exfoliating the epidermis.

Common Errors in the Treatment of Fractures

WITH PARTICULAR REFERENCE TO FRACTURES OF THE EXTREMITIES

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ERRORS commonly observed in the management of fractures, and I am afraid commonly committed by a good many of us, may be classified as follows:

Too vigorous manipulation of the fracture without first securing muscle relaxation by traction. In the great majority of fractures simple relaxation and early traction will reduce the deformity. In my own opinion, manipulation is likely to cause more complications than the initial injury.

Inadequate immobilization of the fracture, with resultant deformity and disability.

Failure to maintain proper weight bearing and the correct carrying angle. Both posterior and medial displacement tend to increase, and are usually both crippling and deforming.

Failure to wash the injured member before applying moleskin adhesive tape. Ordinary adhesive tape should not be used; it frequently tears, and it causes excoriations and blisters. The moleskin should be parallel to the arm or leg to which traction is applied and never criss-crossed. It is secured by an elastic bandage. It should be remembered that skin traction is

efficient only on the humerus and femur; when it is limited to these bones, direct suspension traction is a most important method of securing immobilization. Skeletal traction is indicated on the lower leg or the forearm, and cardinal principles are violated when adhesive traction is applied to them.

An attempt to hold a fracture in the correct position by some sort of pressure apparatus. This usually results in ischemia at the fracture site, and eventual nonunion.

Too early removal of the cast and too early weight bearing in fractures of the lower extremities. Fractures, generally speaking, heal within certain periods of time, but individual fractures do not follow the schedule, and the only way that one can determine what has happened in any special case is by x-ray evidence.

Failure to remember that the initial application of a cast, even with the fracture in good position, does not end physician's responsibility. The position is lost as swelling and edema decrease and disappear, and a new cast is necessary to meet the changed conditions. My opinion is that all fractures, after reduction, should be immobilized either by a posterior mold cast or a three-quarter cast, supplemented by an elastic bandage to provide for reduction in the swelling and edema. At the

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Fig. 1

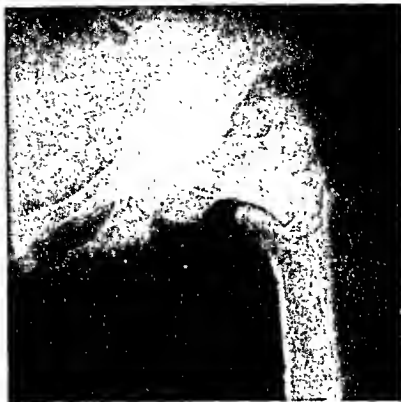


Fig. 2



Fig. 3

Fig. 1. Valgus position for intertrochanteric fracture. Attempts should be made to secure this position. Fig. 2 (center) Coxa vara deformity following intertrochanteric fracture. Poor results follow this position. Fig. 3. Flange for immobilization of fracture of neck of femur.

end of a week or ten days when the edema and swelling have subsided, a second cast should be applied, which at this time can be safely circularized.

Failure to observe, as well as to record, the status of the pulse and the neurologic status of the extremity at the time of initial treatment. The physician will save himself much embarrassment, and patients will be saved much disability, if these simple precautions are always remembered.

Most errors encountered in the treatment of fractures of the extremities are errors of omission. Most of them, as is evident from the brief outline I have just given, would be avoided if only we bore in mind the basic principles.

Bearing these basic principles in mind, let us see how best to avoid common errors in the management of specific bones.

Fractures of the hip and femur—End results in dislocations of the hip associated with fractures of the femoral head or of the acetabulum differ from immediate results. Many times the results seem good, and continue good for a year or two. Four or five years later, however, there is a narrowing of the joint space and eventual aseptic necrosis; that happens in perhaps 90 to 95 per cent of all cases, and we must bear it in mind when we are confronted with patients who have suffered such an injury and must

give a prognosis. When dislocation occurs without fractures, this complication occurs in only about 5 per cent of all cases.

A fracture of the femoral shaft with a wide amount of separation may present two types of deformity to be corrected, posterior displacement and medial angulation. It is always proper to employ traction of 20 to 30 pounds initially and to continue it for a period of perhaps ten days. If at the end of that time reduction is not satisfactory, it is not likely ever to be, and the best interests of the patient demand a prompt resort to an open operation.

FRACTURES of the femur in children with a large amount of overriding are particularly hard to handle unless they are seen promptly. In fact, unless they are seen and treated promptly there is practically no amount of traction which will effect a reduction. The reason is the hematoma present at the fracture site. If it becomes organized, as it does at the end of six hours, it will invade the soft tissue and lessen the coefficient of elasticity, making traction, as a result, a thoroughly unsatisfactory method of management. Surgery should, however, be avoided unless there is soft tissue interposition, or marked overriding of the fragments.

Intertrochanteric fractures are very generally

mistreated, more commonly so, I believe than any other type of fracture. One reason is that in spite of their importance, modern textbooks devote almost no attention to them. Text after text dismisses them with only 5 or 6 lines. The circumstances of treatment, of course, are not easy. The average age of the patient with this variety of fracture is about 67 years. The spine is likely to be arthritic. Coxa-vara deformity is frequently associated with the injury, and the result is usually a shortening of about an inch, for which the spine or pelvis cannot adequately compensate. The patients, if they are not treated with these possibilities in mind, frequently have very severe pain, not in the hip, but in the back.

Objective of treatment of an intertrochanteric fracture, whether managed by traction, with adhesive tape, traction splints or a cast, is that the leg should be approximately an inch or at least three-quarters of an inch longer than the uninjured member, and in a valgus rather than a vara position. If x-rays are compared in which treatment is carried out with this objective and without this objective, the difference in results is obvious. The desired elongation can be secured by changing the angle to a valgus which eliminates at once the undesirable coxa-vara position and the chain of consequences which follow its use.

Another type of fracture which is very common and which sometimes causes trouble is the

intertrochanteric fracture with avulsion of the lesser trochanter. It can be treated just as the usual intertrochanteric fracture, that is, by traction alone; or by traction followed by a body cast. For intertrochanteric fractures without comminution, immobilization by means of internal fixation is satisfactory. If, however, the fracture is comminuted, it is an error to try to use any type of internal fixation; the results are never good.

IMEDIATE application of the maximum amount of weight, that is, 20-30 pounds, not only reduces the fracture, but also reduces muscle spasm and indirectly benefits any state of shock, which may be present. Within a week or ten days after the injury most patients will be relieved of the muscle spasm. When that has been achieved, the precise type of treatment can be left to the desires of the individual surgeon. Closed reduction or open reduction with the application of a body cast gives equally good results.

The type and application of the apparatus are important. The weight should extend free over the end of the bed, so that the patient does not have access to it. A small weight in the center, to give suspension traction, permits the patient to raise himself in bed, making nursing a little easier. The ring of the Thomas splint



Fig. 4. Direct suspension traction.



Fig. 5 (left). Avulsion fracture of greater tuberosity with dislocation of head of humerus. Fig. 6. Avulsion of greater tuberosity following reduction of dislocation. This requires surgery.

should be large; a small ring permits pressure and may result in such unfortunate consequences as a pressure necrosis, especially over the ischial tuberosity, sciatic nerve involvement and thrombophlebitis. The correct weight bearing line should be adhered to, namely, from the anterosuperior spine of the ilium through the patella and extending between the first and second toes. If these precautions are observed, and if slings are placed correctly across the bar, two very crippling and disabling deformities are prevented, namely, a medial angulation and a posterior displacement.

A very common error in the treatment of fractures of the neck of the femur is the incorrect use of pins and wires. If some form of immobilization is to be used for fractures of the neck of the femur, wires should not be used, they will either pull out or bend. The use of a flange, or of two screws, will adequately immobilize the fracture.

AN IMPORTANT rule in the management of fractures of the femur and fractures about the hip joint is that weight bearing should not be attempted for a minimum of six months. The precaution is nothing but common sense. As is very well known, deposition of bone by natural processes takes a minimum of three

months, and another three months is required for the callus to become firm, hard, bone. Some type of ischial non-weight bearing caliper or brace should be employed for another three to six months, following immobilization, for additional protection.

Fractures about the ankle—A fracture of the internal malleolus running across the lower end of the tibia, with angulation at the mortise of the ankle, can produce a deformity that is crippling and disabling. The cancellous bone is usually driven up into the tibia by compression and dorsiflexion, and its removal is practically impossible unless proper early treatment is applied. If a Steinmann pin is inserted early in this type of case, results are usually good. If it is not, the ankle mortise can be restored and proper articulation of the tibia achieved only by osteotomy and transplantation of a portion of the tibia.

Fractures about the shoulder—One very common error in the management of fractures of the greater tuberosity associated with a dislocation is failure to reattach the greater tuberosity to the shaft of the humerus. As a rule, the dislocation has been properly reduced and the circulation and innervation of the region have been checked. (Incidentally, the findings should be appropriately recorded for the phy-

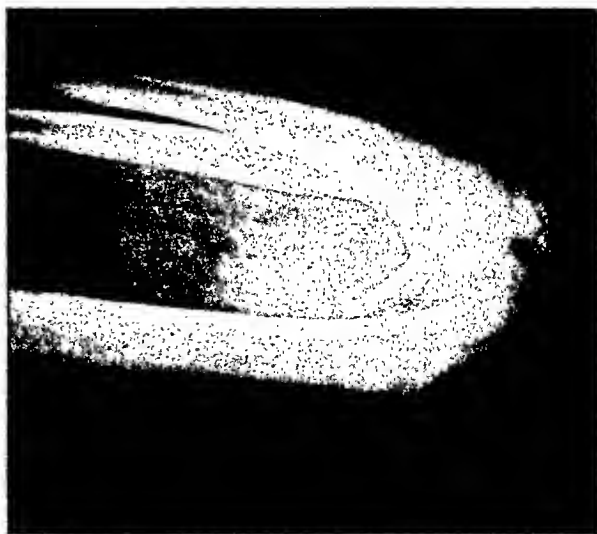


Fig. 7. Comminuted supracondylar fracture. Flexion too acute.



Fig. 8. Oblique fracture of humerus causing radial nerve paralysis. Fig. 9 (center). Screw in olecranon for traction. Fig. 10. Traction by means of screw in olecranon.

sician's own protection at a later date.) Yet often, at a later investigation, there is a concavity at the greater tuberosity, because it has not been reattached to the shaft. This is a serious problem. The external rotators, the infraspinatus and the teres minor attaching to the greater tuberosity are now pulled posteriorly and superiorly instead of externally and anteriorly as normally, and the patient has grossly impaired the functions of abduction and external rotation. If such a situation has developed, the treatment is always surgical. It is necessary to bring the tuberosity back to its normal anterior position, rotate the arm, and then reattach the tuberosity in order to regain the lost functions.

Supracondylar fractures—Textbooks teach that the correct position of treatment for supracondylar fractures of the humerus is acute flexion and supination. That is true, but on the other hand, exaggerated positions of any kind, whether flexion or extension, are to be avoided. Supination and flexion, improperly applied, can completely rotate the distal end of the humerus; the reverse error is failure to apply sufficient flexion to bring the bony surfaces together. It is common practice in these circumstances to blame the circulation. The operator's finger is

kept on the pulse as the forearm is brought up in supination and flexion, which, of course, is quite proper, and immobilization is carried out at the angle; the pulse is regained. Again that is correct.

There is little or no reason, however, why within the next day or two when edema and swelling have lessened, the cast cannot be removed, the elbow flexed farther until the pulse is lost; then by slight extension the pulse is regained and immobilization in that position carried out. After two or three such manipulations the arm can be brought into acute flexion and supination and the deformity present after the first manipulation, because of interference with the circulation, completely eliminated. There is no excuse whatsoever for accepting the protection of the circulation as an excuse for a poor result. A little more vigilance and repeated manipulations, which can be carried out without anesthesia, will eventually result in the optimum position necessary to maintain reduction. I think it fair to say on the basis of my own observations, that some 60 per cent of the cases of supracondylar fractures are reduced at right angle flexion rather than in full supination and flexion.

Another unsatisfactory end result in a supracondylar fracture occurs in the oblique variety. If it heals with excess callus formation, a small spur may form and protrude laterally, the musculospiral nerve will invariably be caught in the fracture, just as it will be caught in a spiral fracture. Should this happen, osteotomy and neurolysis of the musculospiral nerve are the only solution. An oblique fracture, and particularly an oblique fracture which introduces any possibility of involvement of the musculospiral nerve, warrants early skeletal traction, or even surgery.

Skeletal traction in supracondylar fractures—In employing skeletal traction in this area, extreme care is necessary to safeguard the ulnar nerve. The use of a wire across the ulna, or the use of a drill or any other form of skeletal traction, can readily cause an ulnar paralysis, particularly if the nerve is displaced in a comminuted injury. My preference in such cases is to use an ordinary screw hook, such as can be bought in a hardware store for two or three cents. It is placed in the ulna about two fingers' distance from the tip of the olecranon process. A weight is then placed horizontally and traction applied. The forearm is supported with moleskin adhesive tape in a position of supination and flexion. The screw remains in position three or four weeks. If at the end of that time the fracture is not reduced, some other method must be used, but as a general rule even comminuted fractures can be reduced in good position by this simple method, which avoids injury to the ulnar nerve.

Fractures of the olecranon process—These are managed in extension, but one must realize that position is not everything. A fracture managed in the proper position can still show separation between the fragments; the important consideration is how great a tear of the capsule has occurred, just as in a fracture of the patella, in which a tear of the lateral capsule accompanies the deformity. Unless the olecranon is placed in its correct position, a dislocation of the forearm can occur when the elbow is in extension.

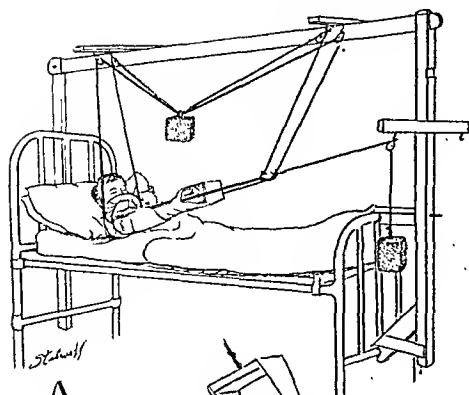
Fractures of the radius and ulna—Fractures of the head of the radius associated with fractures of the ulna, unless properly immobilized; often may produce a most serious type of deformity, with loss of flexion that amounts to a practical ankylosis of the elbow. The best way to handle a fracture dislocation of the head of the radius with a fracture of the ulna is to remove the head of the radius early, split the triceps, and put a screw through the proximal portion of the olecranon anteriorly down into the medullary canal. By this procedure anterior dislocation of both bones of the forearm is prevented and approximation secured. Motion can be started promptly and deformity and dysfunction are avoided.

A COMMON error in cases of fracture dislocation of the head of the radius associated with fracture of the middle third of the ulna is to remove the radial head at an early date without rigidly immobilizing the ulna. If the ulna is not protected by this rigid immobilization, the end result is inevitably bad.

Other difficulties also arise in cases in which the head of the radius is removed when the ulna is also fractured. Sometimes a small amount of callus formation will limit pronation and supination. If the radio-ulnar ligaments are torn at the wrist, shortening of the radius by resection of the head permits displacement of the distal normal radio-ulnar articulation under these circumstances, and the patient has a great deal of pain, not at the elbow, but at the wrist. I had one patient in whom resection of the lower end of the ulna was eventually necessary for relief of pain.

Still another precaution in both bone fractures of the forearm is the proper amount of immobilization of *both bones*, the ulna as well as radius. Indeed, immobilization above the elbow joint is always necessary to prevent marked deformity with loss of pronation and supination.

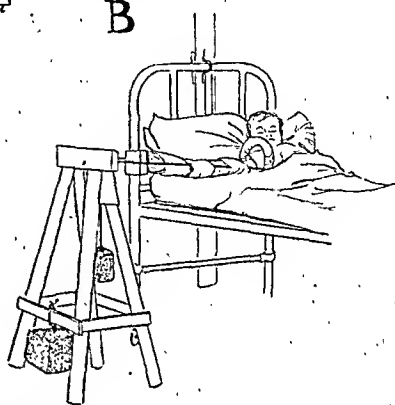
A convenient and a practical method of describing management of both-bone fractures of the forearm is to visualize the forearm in three sections. Fractures in the upper third



A

A. Longitudinal traction on humerus. B. Lateral traction on humerus. C. Conservative traction on humerus with felt. D. Steinmann pin in os calcis. No dressing. E. Block to correct altered weight-bearing line with Steinmann pin traction. F. Posterior mold cast for fractures of tibia and fibula.

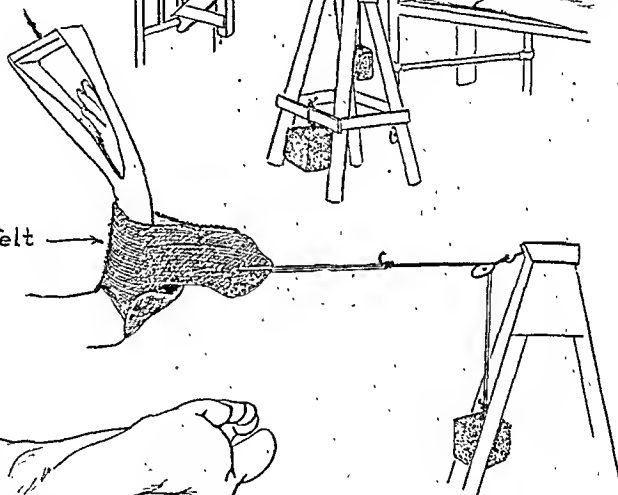
B



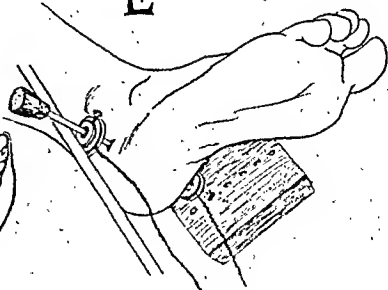
C

Felt

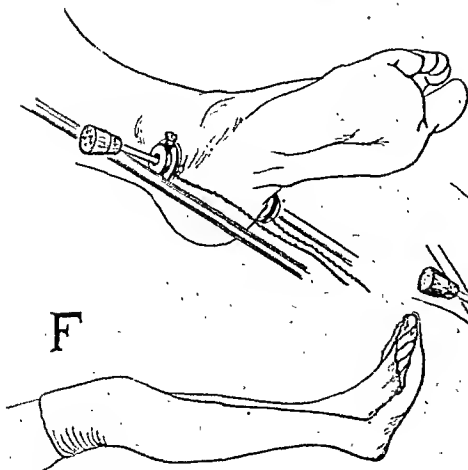
D



E



F



should be placed in supination and right angle flexion. Fractures in the middle third should be placed in midpronation. Fractures in the lower third should be placed in pronation. If these double fractures are placed in the correct position, even though there is overriding, a wire can be inserted through both bones for traction, and both fractures will immediately be immobilized in the correct position. If, however, the wire is inserted before the correct position is assured, the error is merely perpetuated and the position cannot be changed until the wire is taken out.

SOME fractures of the forearm cannot be put into good position by manipulation. A fracture involving the lower end of the radius with slight obliquity, or which is transverse, is almost impossible to reduce by manipulation, particularly if only the radius is fractured and the fracture is at the pronator quadratus. The proper way to manage such a case is by early surgery. The fracture can be "jack-knifed" into position through a small incision, and healing



Fig. 11 (upper). Comminuted fracture of head of radius with fractured olecranon. Fig. 12 (lower). Removal of head of radius. Fracture of olecranon reduced and immobilized by metal screw.

usually occurs rapidly and in excellent position.

Injuries at the wrist immobilized in plaster casts are not always as simple as they seem. I recollect one such case in which the styloid process of the radius was longer than that of the ulna. The distal articulation was normal, pointing forward 10 degrees, but a half-moon shadow in the roentgenogram was overlooked, and the patient, instead of having a Colles fracture, actually had a dislocation of the lunate bone. The proximal carpal row should always be investigated. These bones are likely to be involved in a fracture at the wrist; dislocation of the lunate bone and fracture of the navicular bone form a rather frequent combination. If the dislocation of the lunate bone is left unreduced, median nerve injury can be anticipated.

When a fragment of the navicular bone is dislocated up the forearm, the question always arises as to whether it should be replaced or resected. If there is marked displacement of the carpal bone, resection will inevitably produce a disability, which may be very marked. It is better policy to put the fragment back into position and take the chance that it will not die. A white sclerotic area always makes one think that the bone is dead; invariably it means inadequate circulation and time alone will tell whether sufficient nutrition for revascularization will be supplied. In bone pegging the fracture of the navicular bone, the peg need not be taken from the tibia; it is perfectly practical to take it from the radius, and immobilization is just as adequate as with a tibial peg.

It is a temptation, in dealing with a comminuted fracture of the lower end of the radius, to let severe comminution overshadow every other consideration. A review of the original x-ray may reveal a mere suggestion of a line, rather than a true fracture line, and recheck x-rays often reveal separation because of absorption at the fracture site. It should be axiomatic, in the management of comminuted fractures of the wrist, to pay particular attention to the proximal carpal row, because an overlooked fracture or dislocation may vitiate an otherwise good result.

Developmental Diagnosis of Infant and Child:

ITS ROLE IN CLINICAL MEDICINE

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DEVELOPMENT, as well as disease, falls within the scope of clinical medicine. This simple proposition has far reaching implications for pediatrics, for neuropsychiatry and for individualized public health. And the many general practitioners in this audience know they are constantly confronted by problems of child development. We cannot give adequate medical protection to the growing child, unless we are prepared to diagnose his capacity to grow.

This capacity to grow manifests itself in three major directions:—anatomic, physiologic, and behavioral. First and foremost, pediatrics is concerned with bodily nutrition and with the somatic signs of health and well-being. But this is only a beginning. The basic maturity of the child is manifested in his behavior characteristics—in his ability to use his senses, his muscles, and his total action system to meet the demands of life. A man may be as old as his arteries; a baby is as old as his behavior.

To diagnose development, therefore, we must diagnose behavior. This can be done because the very patterns of the child's behavior are shaped in accordance with deep-seated natural laws. A million years of human evolution have left their imprint on the progressions of child

development. The body grows; behavior grows.

At our Clinic of Child Development at the School of Medicine of Yale University, we have charted the ontogenetic sequences of these basic behavior patterns. Using normal infants as our subjects, we set up a series of test situations designed to elicit characteristic reactions in four major fields of behavior: motor, adaptive, language, and personal-social. All told, we have charted 34 age levels from birth to age ten. In the interest of preventive medicine, special attention was given to the period of infancy. A large group of normal, average infants were studied at lunar month intervals throughout the first year of life. Over a thousand behavior items were listed. This provided us a very finely graded age scale of developmental norms. These norms can now be critically applied as diagnostic criteria to identify behavior in terms of age, and to interpret maturity in terms of behavior.

Let me illustrate the underlying principles and methods with the aid of three cubes. Assume an infant 16 weeks old seated in a washable Morris chair in front of a test table. In actual practice, we use a red one-inch cube which has a universal appeal for the normal infant. The cube elicits a characteristic behavior pattern. It provokes his oculo-motor muscles; he looks at the cube; presently he looks at his own hand; and then again at the cube. This shift of attention makes a behavior pattern. It

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is as observable and as symptomatological as a knee-jerk. It is a behavior symptom which registers a 16 weeks level of maturity. At 28 weeks of age, eyes and hands coordinate to produce a more advanced pattern of behavior. The infant grasps the cube on sight and transfers it from hand to hand—a new kind of attention shift; a higher degree of maturity. At 40 weeks, the range and shifts of behavior are still more advanced; but are just as patterned and as open to diagnostic inspection. The infant seizes a cube with deft thumb opposition; he seizes a second cube; he combines the two cubes, bringing them together by way of adaptive exploitation. At 12 months, he can pick up each cube in turn and release it voluntarily. At 18 months, he builds a tower of three cubes; at 2 years, a wall; at 3 years, a bridge.

EXAMINATION materials shown in the accompanying illustrations are simple in design but effective in their property of stimulating natural, interested behavior. Characteristic behavior patterns are depicted at lunar month intervals, covering the first year of life. These behavior patterns are delineated to show growth trends and a specimen schedule. Diagnostic items for the four major fields of behavior (motor, adaptive, language, personal-social) are listed for the key age of 40 weeks with adjacent listings of developmental items characteristic of 36 weeks and 44 weeks.

Behavior patterns typical of 40 weeks are: exploitation of the cube, extension of the index finger, banging and alertness to the social environment. The exploitation is more diversified when two cubes are offered. The cubes are brought into relation, matched and contacted. The child gives definite attention to the two

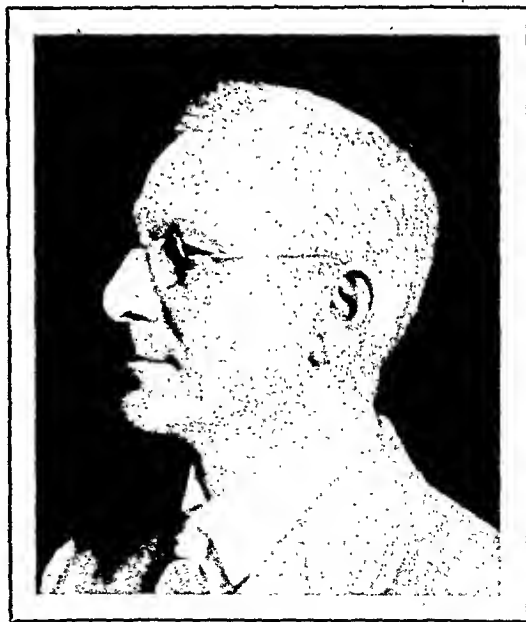
cubes, something he could not do at 28 weeks. Though the child gives heed to the third cube, he holds to the cubes in his hand. All this exploitive behavior certifies to the child's normality.

In the pellet situation, the child succeeds in momentarily grasping the pellet. The characteristic index finger, distinctive of this age, again comes to the fore when he pokes the pellet in the bottle. This is a clear-cut neurological sign, a maturity indicator. He gives special heed now to the bottle, now to the pellet, but is unable to insert the pellet in the bottle.

Given a bell, the child seizes the handle indiscriminately at the top, waves it, spontaneously pokes at it.

When offered a string and ring he adaptively plucks the end, tugs it to the proper distance, exploits the ring and string diversely in a manner which satisfies the developmental norms of behavior for this age.

The developmental examination includes a test and inspection of postural abilities. At 40 weeks supported standing is characteristic and the child also shows a capacity to sit independently.



Arnold L. Gesell

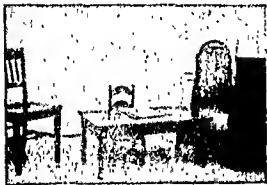
A cinema was shown delineating the behavior patterns of a normal 40 weeks old infant. For clinical comparison and differential diagnosis, the author presented an excerpt of the record of another 40 weeks old infant whose behavior has been distorted and reduced by cerebral palsy—a minimal, selective birth injury from trauma.



A., B. High chair used at fifteen months and for older children unable to sit without extra support; examining table. Note method of attachment to chair. Height of table is adjustable.



C. Room arranged for examination with high chair.



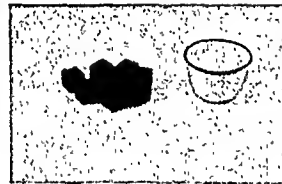
D., E. Standard examination setup.



F. Picture book on table.



G. Cubes.



H. Cup and cubes.



I. Pellets and bottle.



J. Paper and crayon.



K. Formboard and blocks.



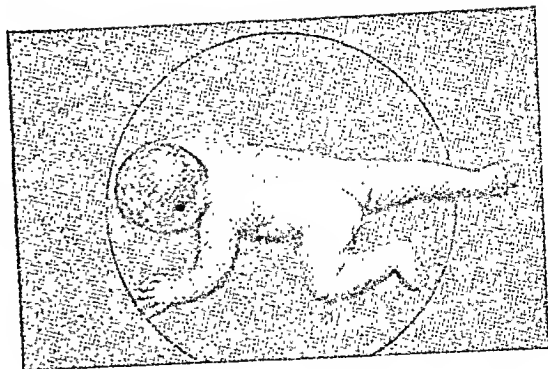
L. Performance box and square (facing child).



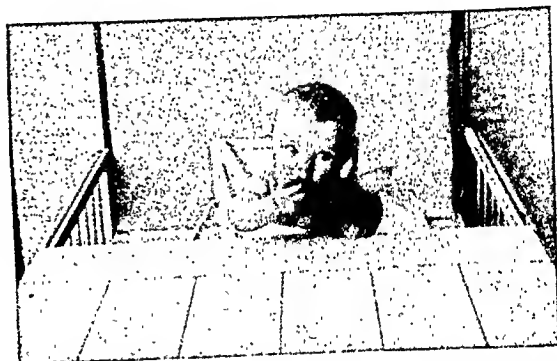
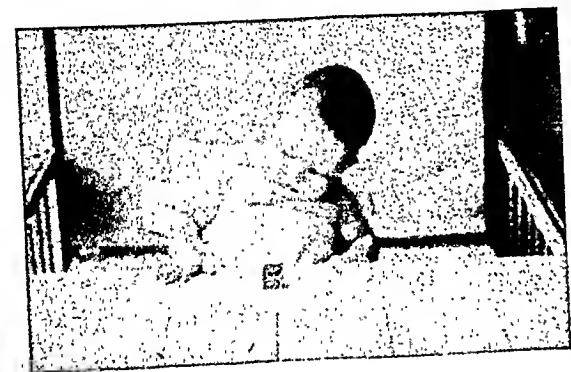
M. Puzzle box and ball (facing child).

Gezell: The First Five Years of Life (Harcourt).

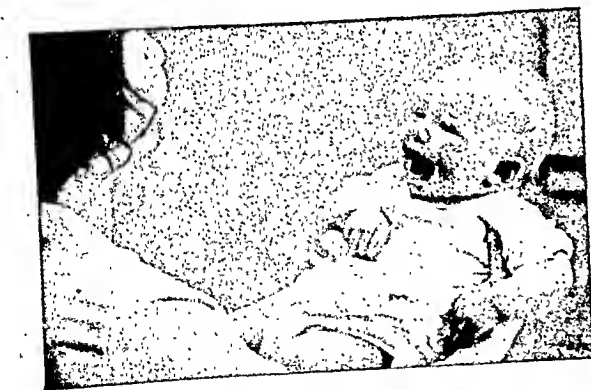
Examination Materials Used In Developmental Diagnosis



Motor



Adaptive



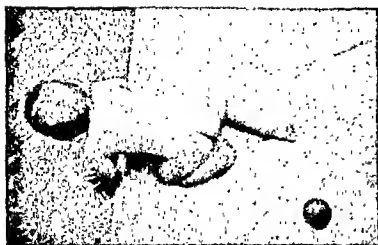
Language



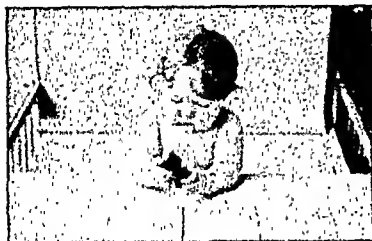
Personal-social

First Quarter: 16 Weeks

Second Quarter: 28 Weeks.



Motor



Adaptive



Language



Third Quarter: 40 Weeks.

Personal-social

Gezell: The First Five Years of Life's (Hager-)

Fourth Quarter: 52 Weeks.

components, and makes possible differential diagnoses of normality, defect, and deviation.

3. It reveals neurologic defects and sensory handicaps, not disclosed by ordinary methods of clinical examination.

4. It supplies important objective information concerning the integration of behavior and the organization of personality.

Consider the innumerable clinical situations where a medical decision must be made, which involves all four of the factors just mentioned.

A foundling or a foster infant is offered for adoption. What is the developmental outlook of this infant? A developmental diagnosis alone can reduce the risks of adopting a baby.

An infant is prematurely born, perhaps with episodes of cyanosis and apnea. Will he develop normally? A diagnostic study of behavior will soon tell.

Another infant has suffered a birth injury. Was the injury slight or grave, is it selective or devastating? Should he have physiotherapy?

A preschool child is referred for tantrums and slow speech. The developmental examination reveals deafness, hitherto altogether unsuspected.

AND so we might list an array of conditions in which development and disease simultaneously fall within the scope of clinical medicine: simple amentias, aplasias, malformations, degenerations, traumata, infections, anoxemia, erythroblastosis, endocrine dysfunctions, excessive emotional stress, environmental retardations, and pseudo-symptomatic syndromes.

All children, normal and abnormal, are continuously confronted with the universal problem of development—the problem of growing up. We cannot give adequate protection to these children, particularly in the first five years of life, unless we provide developmental diagnosis and developmental supervision at periodic stages of their growth career.

The untrained physician cannot make a conclusive developmental diagnosis. He can, however, be alert to the behavior symptoms of in-

fant and young children in private practice, in his well-baby conferences, in child-health centers, and in child care agencies and institutions. At the lowest minimum there should be a routine *behavior inventory* which will screen significant defects and deviations. At the higher levels of medical organization, in hospitals and at teaching centers, there should be facilities expressly designed for the diagnostic study of complex cases of maldevelopment, and for the developmental supervision of handicapped infants throughout the whole preschool period.

These specialized facilities should have a separate locus, appropriate equipment and a trained personnel on a par with other diagnostic departments.

We have established specializing externships in our clinic in which the extern devotes one or two years to the methods and procedures of developmental diagnosis on a full time service.

Developmental diagnosis is becoming a specialty in the domain of pediatrics. This is its logical orientation, since pediatrics is in itself a generalized form of medicine, which by tradition and necessity deals with the total child in his natural cultural setting. Neurology, orthopedics, and psychiatry also are concerned with children, but primarily from the standpoint of impaired or abnormal functioning. Child psychiatry, in so far as it represents a downward extension of adult psychiatry, lacks the concepts and methods which are essential for the developmental diagnosis and supervision of newborn and growing infants. Developmental pediatrics, in contrast, begins with birth and moves forward with the progression of the growth cycle.

Pediatric medicine is supervisory as well as diagnostic. It begins with the regulation of nutrition and physiologic well being, both of normal and abnormal babies. In view of new scientific advances, we may be certain that the somatic aspects of human growth will be brought under increasing control, together with undreamed of refinements of physical measurement and assay.

Organic Variability in Heart Disease

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ABOUT forty of every hundred doctors die from some form of coronary disease; of these, the majority from coronary thrombosis. It may therefore be of interest to physicians to consider some of the common factors involved in the acute episode and to inquire whether there is anything that we doctors can do to avert this common fate.

I shall limit the discussion to coronary thrombosis and emphasize that coronary thrombosis may occur in a myocardium that reveals no vascular degeneration; and that thrombosis of the coronary vessels is favored when the current is sluggish, coagulation time accelerated, and the endothelium is unduly adhesive. This constellation follows a period when blood pressures have been higher, the current more rapid, the coagulation time slower, and the endothelium less adhesive.

The temperature zone in which we live is characterized by great variability in weather conditions and by a wide range and rapid



William F. Petersen

changes in temperature. Such direct environmental factors become of great importance in conditioning the state of the organism. Of importance is the fact that the effect of weather may be cumulative, particularly in spring and fall.

THE CLINICAL RECORD

Turning now to the clinical record, we find that coronary thrombosis is in fact characteristically seasonal, its highest incidence during

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the periods of the year just mentioned, and, in addition, is weather-conditioned, occurring most often at temperature extremes—that is, during periods of unusually high or low temperatures, and most often after periods of cold.

Coolidge—Mr. Coolidge died suddenly on January 5, 1933. He was apparently in good health, though he had complained of hyperacidity for several days. Mr. Coolidge was allergic and poorly buffered; he tired easily and reacted markedly to any change in biotonus. Merely stepping onto a boat would make him seasick; cold weather promptly brought on a "sour stomach." The reason for the sour stomach that so frequently bothered him was simple. With the passage of each cold air mass we are apt to have a relative anoxia in large areas of the body as a result of vasospasm. This in turn leads to the compensatory production of capillary active substances such as histamine, more carbon dioxide, etc. The histamine acts on the stomach mucosa, thereby producing more hydrochloric acid. At these times, Mr. Coolidge would take soda, as do many others under similar circumstances.

Keeping this in mind when we study the temperature at the time, we note first a severe cold wave that sent temperatures down 60° F. in a day. Consider for a moment what this would do to the vascular system of a sensitive organism such as that of the former President. The peripheral vascular bed would contract maximally (insulation) and the pressures would rise abruptly. The load on the heart would be greatly amplified.

Then the reversal would follow along with capillary active substances being formed in the regions which had been anoxic. The capillaries would dilate; acid production would reach a peak; the vessel walls would be sticky; coagulation would be enhanced; and blood pressure would fall.

Then the environmental temperatures rose just as abruptly as they had fallen a few days before. Such an increase in the temperature would be followed by peripheral dilatation of the vessels, and this, too, would lower blood

pressure. We would then have two similar trends, the one amplifying the other: (a) the biological after-effect of correction or even over-correction of the preceding cold wave, and (b) the normal effect of the warm wave. The result—very low blood pressures, unduly sticky vessels, shortened coagulation time, and blood concentration. With that state could come sudden clotting in any area actually or potentially inadequate, such as the coronary and cerebral regions and occasionally in the extremities.

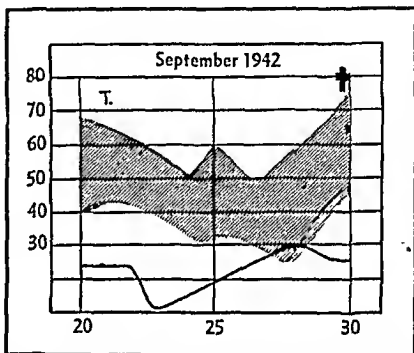


Fig. 1. Meteorogram with daily maximal and minimal temperature for Minneapolis, September 20-30, 1942. Death of Dr. Gortner occurred on the 30th.

F. D. Roosevelt—Mr. Roosevelt reportedly had a very severe cerebral episode at Hyde Park, New York, on March 25, 1945, and was hurried to Warm Springs, Georgia. The final blow came on April 12. An examination of the weather record shows that at Hyde Park, the temperature had reached the eighties in mid-March and declined sharply to freezing levels by the twenty-second. Then came an up-swing with an occluded front (i.e., temperatures up and barometric pressures also increasing) and under these weather conditions, Mr. Roosevelt experienced a serious cerebral accident, a "stroke."

At Warm Springs there was a related situa-

tion. It was almost freezing on the seventh of April; then an upswing of 40° F. and, with this, the terminal episode. Thrombosis, followed by rupture and hemorrhage, was probably the immediate cause, but since we do no postmortems on our presidents, we cannot be absolutely certain.

Gortner-Palmer—On September 1, 1942, Dr. Ross A. Gortner, well-known Minnesota chemist, wrote me, and made one or two statements which I think are of interest. "I have always



Dr. Ross Aiken Gortner,
1885-1942.

contended that a single determination of a blood analytical value is relatively meaningless, since observations in our own laboratory have indicated wide variations from day to day. Most of our observations have been made on the blood of animals and perhaps meteorological conditions are the reason for some of the variations we have observed and which we could not otherwise explain. We have noted major fluctuations in blood phosphorus in dairy cattle on a uniform diet and under as nearly controlled conditions as we were able to maintain. Perhaps this is one of the reasons for my feeling so exhausted on certain days when I think I should be more normal. Ever since I had a coronary thrombosis, high humidity and extreme cold both markedly lower my ability to walk or make any physical exertion."

Dr. Gortner died twenty-nine days later. When we examine the temperature record for Minneapolis, we observe that a sharp decline in temperature had occurred after the twentieth, reaching a low on the twenty-seventh; then the temperature rose rapidly to a crest on the thirtieth.

Dr. Gortner was succeeded as chief of the division of agricultural biochemistry of the University of Minnesota by his associate, Dr.

Palmer. On February 25, 1944, Dr. Palmer had a sudden coronary thrombosis and died on the ninth of March. The Minnesota temperature records indicate that a polar crest was reached on the eighteenth (-10° F.), followed by a rise of 55° F., and at the crest, thrombosis occurred. Death came when the succeeding zero wave increased the cardiac load on the damaged heart.

Edsall—We return to New England for a moment and to our own profession. In the *Journal of the American Medical Association* (V.128, No. 17) we find the obituary of the Dean of the Harvard Medical School, Dr. David Edsall. He died suddenly on August 12, four months after the death of Mr. Roosevelt. We find that the environmental picture was identical. It had been relatively cool early in the month; then came a sudden rise to almost 90° F. and with that, death! But when Edsall died, Hugh Cabot also died suddenly. Coincidence? No, merely inadequate adjustment to an environmental situation. Actually, death is always due to this, but the specific environmental condition may vary!

Bassac-Bowen—We turn to Chicago; the month is November. An old friend and valued

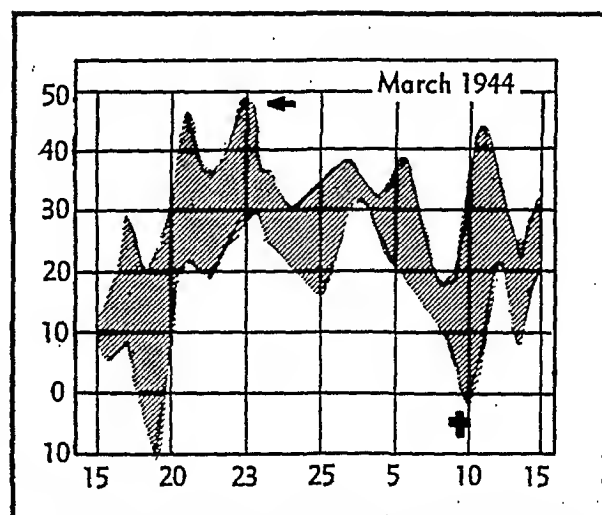


Fig. 2. Minneapolis temperatures associated with the coronary thrombosis, February 25, and death of Dr. Palmer, March 9, 1944.

colleague, Dr. Peter Bassoe, died on the fifth of the month from a sudden coronary thrombosis. He had had a previous attack some years before but had made a satisfactory recovery and had continued in practice, though with some restriction of activity. The meteorogram shows a great temperature decline from over 70° F. to the low 20's. Early in November Dr. Bassoe experienced prostatic difficulty (smooth muscle is shortened with periods of cold and obstructive symptoms are apt to become more pronounced) and entered Presbyterian Hospital for surgical relief. On the following day he died from a coronary thrombosis.

Another friend, but a much younger man, Dr. Bowen of Houston, Texas, was then in Chicago attending a meeting of the College of Allergists. During the same environmental conditions that had terminated the life of Bassoe, Bowen suffered a severe coronary attack. Fortunately he made a good recovery.

Herrick's first case—Inasmuch as Herrick of Chicago was the first to recognize the clinical picture and the first to realize the importance of the clinical entity that we associate with coronary thrombosis, it is of interest to study his first case in relation to the weather of the time. Again we find a characteristic picture. A severe

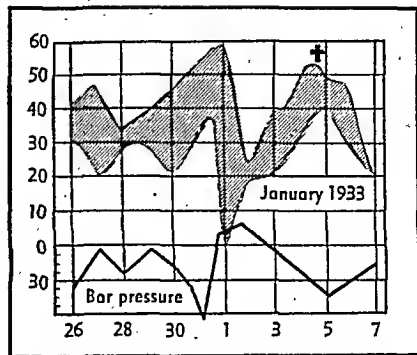


Fig. 3. Environmental temperatures associated with the sudden death of Calvin Coolidge, January 5, 1933.

cold wave had sent the temperature below zero and this had lasted a week; then the rise and with its crest, a coronary attack.

Heninger and Dickens—We can, as a matter of fact, select any case record at random and, with a few exceptions, observe this association of a characteristic environmental pattern and the acute attack of thrombosis. But I would stress that, while the organic state associated with and following temperature swings of the

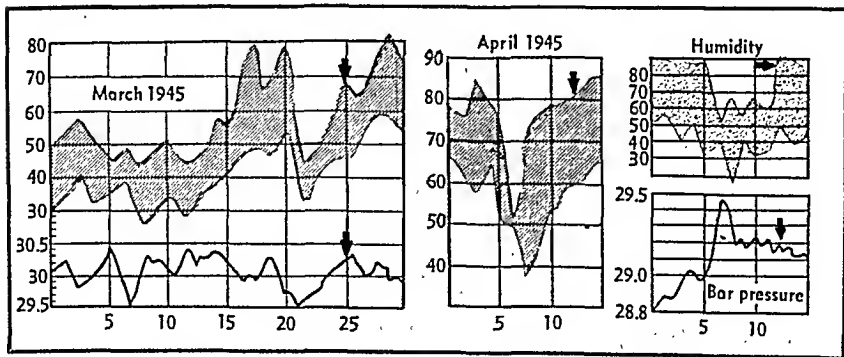


Fig. 4. Meteorograms to illustrate the weather at the time of the cerebral episode of March 25th and the death of President Roosevelt at Warm Springs on April 12, 1945.

type I have here illustrated is of major importance in most cases, other impacts, physical as well as mental, must not be disregarded. Such impacts frequently cause violent alterations of the organic balance, with a marked sympathicotonia that may be followed by an equally great reversal in biological mechanisms concerned—chemical, endocrine, nervous, physical, etc. Depression from grief or worry, irritation and anger, exertion and fatigue; digestive overload;

no abdominal distension. The following morning he suffered severe precordial pain radiating to the shoulder and down both arms to the fingers.² He was very restless and his respirations were somewhat rapid and labored. The pain was so severe that $\frac{1}{4}$ grain of morphine was given; this was repeated in a half hour, with some relief. His temperature was 99° F. the night before admission. The patient had had a similar attack 25 years previously. He

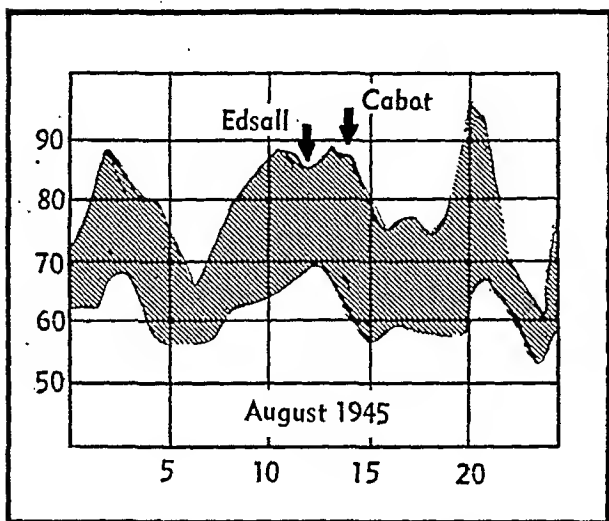


Fig. 5. Meteorogram to illustrate the environmental temperatures (daily maximal and minimal) associated with the coronary episodes in Drs. Edsall and Cabot.

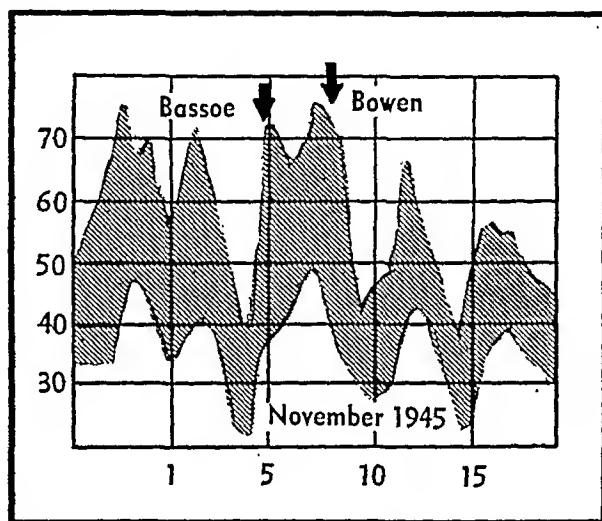


Fig. 6. Meteorogram to illustrate the environmental temperatures associated with the coronary episodes in Drs. Bassoe and Bowen.

infection and intoxication—all these must be kept in mind in the clinical observation and control of the patient.

Heninger and Dickens have published a case record that will serve our purpose. (Reference numbers correspond to numbers in meteorogram.)

"The patient, C. R., white male, aged 56 years, was admitted to the Touro Infirmary, March 22, 1937, 5 A. M., in a stuporous condition.³ The history was obtained from his wife and family physician. The chief complaint was precordial pain. Four days previous to admission, the patient consulted his physician complaining of gas on the stomach. His blood pressure was 130 systolic and 70 diastolic; there was

gave no history of venereal disease.

"Physical examination: Blood pressure was 60 systolic and 40 diastolic; pulse 70 and irregular. The pupils were contracted. Breathing was rapid and irregular. The tongue was coated; head, neck, lungs and abdomen were negative. The heart sounds were distant and irregular; no murmurs were heard. There was slight cyanosis of the fingernails.

"Course: An electrocardiogram was taken on admission revealing complete heart block. Caffein sodium benzoate gr. $7\frac{1}{2}$ and morphia gr. $\frac{1}{4}$ were given one hour later. At 9:30 A. M. the patient became cyanotic and was cold and clammy. Pulse was not felt. Heart beat could not be heard. Temperature was 102° F.

The patient died five hours after admission."⁴

The metcorogram for New Orleans illustrates the characteristic situation: first, a cold wave with a 40° drop in temperature, then the upswing and with it, thrombosis.^{1,2} The myocardium was badly damaged as a result. Three days later another cold wave and, with this, greater arterial pressure and greater intracardiac pressure. Then, death on March 22.^{3,4}

A PSYCHOSOMATIC INTERPRETATION

While I would not for a moment deny the integration of the psyche and the soma and indeed have for many years stressed the need of considering all factors in the total clinical picture if we would understand medicine, I do on occasion become a bit annoyed at the carry-over of the verbal refuse of the psychoanalytical epoch into a field that should be wholly freed from this blight. Psychosomatic medicine should not be another specialty; it should be common property of every real physician, but it certainly is not heading in that direction at the present time. For instance, here is Dunbar's formulation of the coronary case:

"They have a general air of self-sufficiency and tend to dominate in social relationships through superior argumentative skill. They

rarely allow themselves freedom in emotional expression but talk readily about themselves and describe their own feelings insofar as they can find some respectable formula or predecessor for them through Schopenhauer or the Bible.

"Accepting the idea of hierarchy, they identify themselves with authority figures and strive to become superauthorities. Unlike the hypertensive, they make up their minds quickly because they have a definite frame of reference in their long-range goal. The resemblance to the fracture patient is only superficial because a fracture patient's decisiveness is based upon a response to immediate values.

"The coronary accident in these patients is precipitated by an apparently irreparable mutilation of their picture of themselves because of external threats to their authoritative role.

"Their initial reaction to illness is despair combined with a compulsive need to deny any need for change in their pattern of living, hence their tendency to overdo and disobey instructions or to develop extreme depression.

"This personality constellation plays an important role in bringing about the coronary accident and has a bearing on prognosis and therapeutic management. In the typical extensive coronary patient, the prognosis will be relatively poor unless some appeal can be made to his creative impulses. Emphasis should be laid on a creative outlet still open to them without accentuation of the necessary curtailment of their usual activities."

THE VASCULAR REACTION

Now let us keep to the simple facts. In Fig. 9 I have sketched the changing blood distribution, or blood balance, that is of basic importance for our consideration and for the understanding of many clinical conditions.

The figure in the center represents the normal equilibrium of the blood distribution. The effect of cold is illustrated at the left (insulation-sympathicotonia). At the right we have peripheral dilatation i.e., radiation with, in general, lowered pressures.

A schematic illustration—We can illustrate

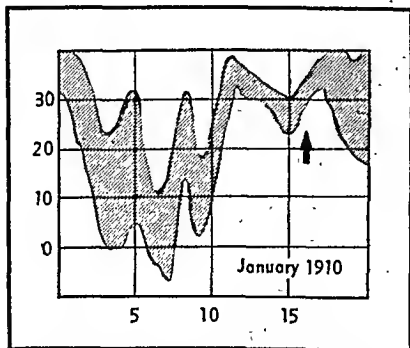


Fig. 7. Chicago environmental temperatures, January 1910, to illustrate Herrick's case No. 1. Arrow points to date of coronary thrombosis.

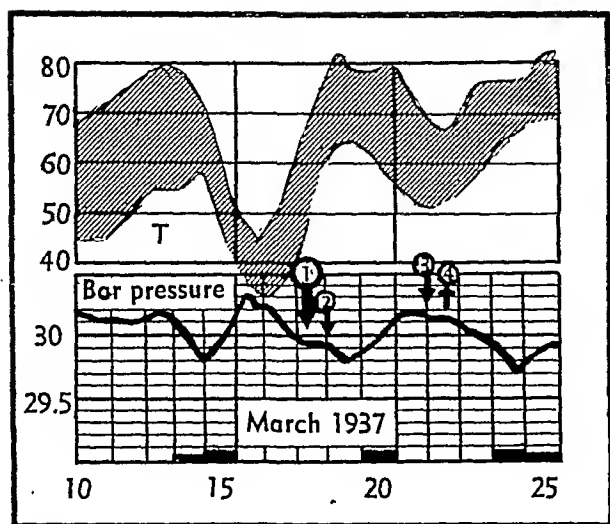


Fig. 8. Meteorogram for the period in March 1937 (New Orleans) associated with the coronary episode in the case of Drs. Heninger and Dickens.

this organic rhythm very simply if we merely diagram blood pressure levels, as in Fig. 10. At the arrow, an energy impact occurs—it may be a cold wave, an emotional upset, exertion, infection, or an allergen. A sympathicotonia follows—vessels constrict, pressures rise; it is an “alert” or “adrenal” phase, if you so wish to designate it. Selye termed it the “alarm reaction.”

If at this time the skin is tested, flares are negligible; there is greater resistance to infection; cells are temporarily less permeable. A relative alkalosis and hyperglycemia exist, together with an increase in blood pressure.

This adrenal or “stop” phase changes to the “go” phase—vessels dilate; there is relative acidity; cells become more permeable; they are less resistant to injury; skin flares are exaggerated.

All this is very simple. Assume now that we must equilibrate two such impacts in rapid succession (1 and 2 in the central diagram). Then the pressor level will be higher and also lower, and if later (2) another factor, such as undue heat, supervenes, the pressure may fall to unusually low levels. Or, if with seasonal accentuation, a series of impacts supervene in rapid succession, we will face the situation in

the third diagram, with periods of great pressure crests and depressions in close sequence.

What has been illustrated here for blood pressure holds for every component in the complex series of organic balances.

This blood balance is normally well maintained; but if an autonomically unstable individual or a dysplastic or a sick individual, is placed in an unstable environment (i.e., the storm track area of North America) it will be found that there is a constant pendulation of vasomotor, endocrine, and chemical balances that may reach amazing amplitudes. In Fig. 11 I have charted the day-by-day blood pressure curve of such a patient when observed from May, 1934, to the following May, 1935. The seasonal trends are well defined, (S) reflecting the summer decline, (A) the autumnal crest (relative alkalosis), and (J) the decline of fatigue after the winter crest and its associated anoxia. A period such as this would obviously increase the hazard of thrombosis.

Obviously coronary thrombosis can occur at any time; but during periods of seasonal transition, when we change from winter to spring or from summer to autumn, the opportunity will be enhanced for the simple reason that the

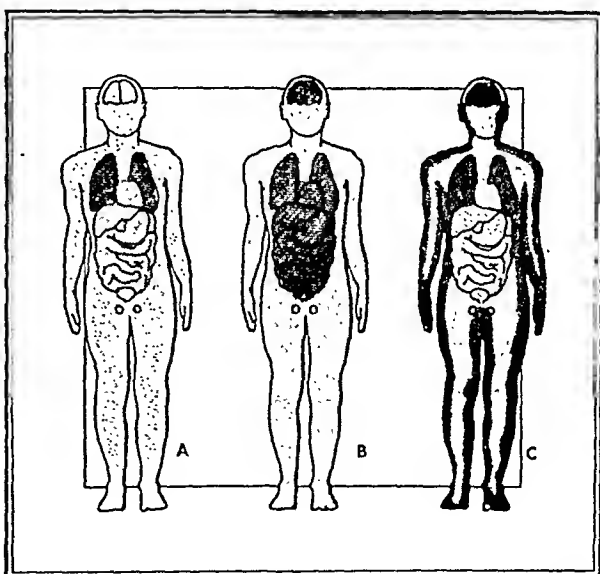


Fig. 9. Diagram illustrating blood distribution with opposite environmental situations: (A) normal balance, (B) cold, (C) warmth.

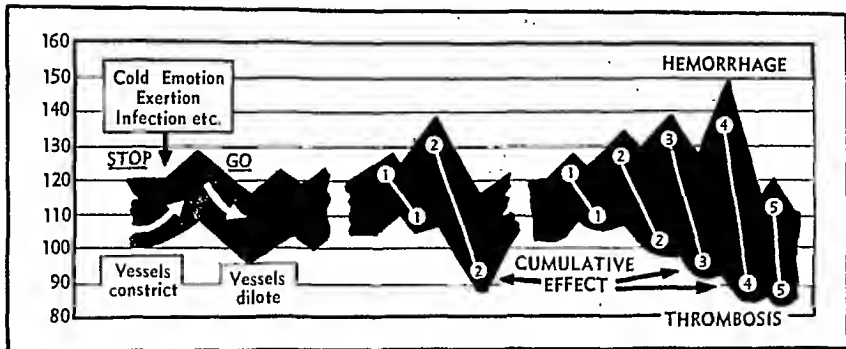


Fig. 10.

autonomic tone is subjected to greater strain.

In broad terms, coronary inadequacy and the final picture of coronary thrombosis merely reflect undue environmental demands on circulatory adjustment. Irrespective of the nature of the environmental demand—heat or cold, work or excitement, digestive overload, or the innumerable impacts which we have to meet—the basic mechanism is identical, modified of course by pre-existing changes in the coronary circuit, kind of person, age, sex, habitus, and familial background.



Fig. 11. Daily systolic and diastolic blood pressure readings, May, 1934, to May, 1945.

But of all the factors and impacts to which the circulatory mechanisms must adjust, for us, living in a region of great meteorological variability, weather is for practical purposes the most important. In maintaining its heat balance most tenaciously, the organism must rely mainly on the circulatory system to shunt the blood to and fro in the major blood beds. As long as we must adjust to violent shifts in the air mass in which we exist, we will tax the vasomotor mechanisms to the limit and in so doing it will be inevitable that coronary dysfunction and coronary thrombosis will occur. In closing I would like to have you keep in mind the statement of Hippocrates, the world's first great physician, "So in one place it stops (i.e. the blood), in another it passes sluggishly, in another more quickly. The progress of the blood through the body proving irregular, all kinds of irregularities occur."

Treatment of the Disorders of Speech

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WE HEAR a great deal in these postwar days about rehabilitation, and rightly so. But we associate the word primarily with the physically ill, with those who have lost an arm or leg, or are blind or deafened. Seldom do we associate it with speech and voice sufferers, although they probably constitute the largest single group in need of rehabilitation today.

It is conservatively estimated that there are over ten million men, women, and children in this country who have some type of speech disorder or voice abnormality. Until recently, these people have been sadly neglected by the medical profession—because the physician, when he came in contact with them, was aware only that they did not speak correctly and tacitly assumed that the solution to the problem was simply a matter of reeducation, and hence outside his domain. What he did not understand, and what I wish to stress in this article, is that a speech or voice disorder rarely develops as an isolated phenomenon but, in the vast majority of cases, is a peripheral manifestation of some underlying psychic or somatic involvement.

The acquisition and subsequent retention of normal speech are contingent on many factors: a normal peripheral mechanism, which, of course, includes the breathing apparatus; ade-

quate hearing; the necessary degree of intelligence; the integrity of the cerebral areas and nervous connections concerned with speech; and an environment conducive to the development of normal speech. Also, there is the vital factor of the emotions. Finally, the endocrine glands should be mentioned, for they not only influence the emotions but in some cases directly affect the development and functioning of the speech organs themselves, particularly the larynx.

Obviously, an abnormality of any of these factors, faculties, and mechanisms concerned in the development and execution of speech, will affect that function, and it naturally follows that the speech and voice specialist is confronted with a multiplicity of syndromes. In the interest of simplification, we usually consider them under five major categories: *dysphemia*, or stuttering; *dyslalia*, or defects of articulation due to faulty habit, environmental factors, mental retardation, or abnormalities of the peripheral mechanisms concerned with the acquisition and execution of speech; *dysarthria*, or articulatory defects due to neurological involvements; *dysphasia*, or language disorders, due to involvements of the language areas of the cerebrum; and *dysphonia*, or voice disorders.

DYSPHEMIA

Stutterers undoubtedly comprise the largest single group of speech and voice sufferers. Dysphemia, or stuttering, is a disorder charac-

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terized by repetitions, blockages, or other interruptions in the flow of speech—and is often characterized also by adventitious movements, such as tics or twitches, especially of the face. It is a psychosomatic condition, for the speech disturbance itself is the symptom of a far-reaching personality disorder. It begins typically in early childhood, and there are many conflicting theories regarding its etiology, their fundamental theses depending upon the orientation in medicine, psychology, or education of their respective proponents. Evidence, however, strongly suggests that the disorder is based on a constitutional predisposition to emotional imbalance in general and to stuttering speech in particular. This constitutional susceptibility—which, incidentally, appears to be on an hereditary basis, since approximately 65 per cent of patients give a family history of stuttering—does not in itself cause the disorder. The speech disturbance appears to be precipitated by emotional shock which may result from an accident, a fright, some radical change in the environment, the advent of a younger child into the family, or the accumulated impacts of a neurotic home environment.

The child who is predisposed to stuttering in most cases demonstrates, even before the onset of the speech symptom, a tendency toward excitability and exaggerated response to stimuli. Soon after the appearance of the stuttering symptom he begins to realize that he is "different" from other children and develops a keen sense of inadequacy, particularly if parents lay undue stress on his poor speech. As he begins to pay the penalties attached to stuttering, his feelings of inadequacy are intensified and give rise, in turn, to morbid anxiety—the child anticipating speech failures and the failures, when they inevitably occur, increasing his anxiety. He is caught in a cycle which eventually leads to the development of a neurosis that warps the entire personality.

For therapeutic purposes, we distinguish two phases of stuttering: the primary stage, before the child has become acutely aware of his disorder; and the secondary phase, when he has



James S. Greene

developed anxiety symptoms and other characteristic personality deviations.

THERAPY in the initial phase of the disorder is essentially a matter of eliminating environmental stress and of helping the child to overcome his disorganization through a regimen of rest, relaxation, and "slow-easy" activity.

It is the secondary phase of the disorder which presents the major therapeutic problem, since at this stage we are dealing with a full-fledged neurosis. The goal of treatment is essentially to break down old, unsound emotional reactions, habit patterns, and attitudes, and to replace them with healthy, constructive new ones—in other words, to build a more mature, more adequate, and more stable personality. This demands a multiple treatment embracing medical, social, psychiatric, and reeducational procedures. Major emphasis, however, is on group psychotherapy. This is because the adult stutterer suffers from a social neurosis—i.e., it is the social setting, the introduction of others into the milieu, which brings the speech disorder to the fore—and group therapy gives

him an opportunity to "act against" his anxiety and his speech symptom in the type of environment which ordinarily elicits them.

The new patient is placed in what might be termed a low-pressure group, in which the seemingly hostile aspects of the outside world which constitute such mental hazards for the stutterer have been for the most part removed.



Patient who has undergone laryngectomy showing opening into the trachea.

As he adjusts to the group milieu, he progresses to more advanced groups. The environment is so devised as to submit him to a gradual increase in environmental pressure in proportion to his growing ability to withstand it. Group therapy is supplemented by individual interviews, the amount of individual work depending upon the specific needs of the patient, and by such supportive group measures as club activities, dramatics, and dancing.

DYSLALIA

The dyslalias, the second major category of speech defects, include delayed speech, lisping, cleft-palate speech, and all defects of articu-

lation other than those due to neurological conditions.

The dyslalias are in general of less concern to the physician than the other types of speech and voice disorders because treatment is largely a matter of speech training and, except for those cases in which organic abnormalities are responsible for the speech defect, is principally the concern of the speech teacher or clinician.

Among the organic abnormalities which affect articulation are various defects of the tongue, although such conditions have a less serious influence on the speech function than might be supposed. Despite the fact that the tongue is popularly considered the principal organ of speech, it can be completely extirpated without greatly impairing speech production.

Clefts of the lip and palate, especially of the latter, have much more serious effects on speech. There are, of course, various types of clefts, some being confined to the hard or soft palate alone and some extending completely through both palates and through the lip. Regardless of type, almost every cleft of the palate has a marked influence on speech, the most noticeable effect being the unpleasant nasality which results from the uncontrolled escape of air into the nasal chambers. This is one of the most difficult defects to eradicate.

Whenever feasible, a cleft of the palate should be closed by surgical measures, and the physician should make every effort to repair the palate in such a way as to insure its best possible functioning for the production of speech. I emphasize this point because the novice in operating occasionally fails to take into consideration the effects on the speech function of cicatricial tissue contraction. The scar tissue in healing tends to contract, thereby restricting the mobility of the palate and almost inevitably foreshortening it and leaving a wide postnasal space. The larger this space, the more difficult it is for the patient to control the escape of air into the nasal cavity, and hence the more pronounced his nasality.

When it is impossible to close the cleft by surgery, the only alternative, of course, is to fit

the patient with an obturator in order to effect closure. However, regardless of whether the cleft is closed surgically or by mechanical means, in almost every case the patient requires speech training. Such training should begin as early in life as possible.

DYSARTHRIA

The dysarthrias are also defects of articulation, but they are defects due to central nervous system involvements which affect the innervation and coordination of the speech musculature. Pathological changes at any one of a number of sites may result in dysarthria. For example, lesions of the lower motor neurones that directly innervate the peripheral muscles of speech—the seventh, ninth, eleventh, and twelfth nerves—will cause a partial or complete paralysis of the parts subserved by the affected neurones, with a resultant articulatory disturbance. Similarly, lesions in the cerebellum or injury to the cortical neurones of the speech areas and the corpus striatum will also cause dysarthria.

The symptomatology varies, depending to a great extent upon the site of the lesion. Speech may be completely absent, as in the case of a bilateral paralysis of the vocal cords; it may be nasal, as in the case of paralysis of the palate following poliomyelitis or diphtheria; it may be labored, scanning, and monotonous; or it may be muffled and indistinct. Often it is hesitant, jerky, and tremulous, and the patient may have particular difficulty with sounds which require intricate muscular coordination. Anxiety usually increases the severity of the disturbance. In some instances, notably in many cases of spastic paralysis, speech may be accompanied by grimaces and various extraneous bodily movements.

PROGNOSIS depends upon the site, severity, and nature of the pathologic changes and upon whether or not these changes are progressive. If the disease process is not progressive and if the patient is mentally alert and cooperative, speech training and muscular reeducation will

usually bring about varying degrees of improvement. Specific remedial procedures must be adapted to the individual case, but the general therapeutic program should embody relaxation exercises, training in muscular coordination and control, breathing exercises, and voice and speech training suited to the individual needs of the patient.

DYSPHASIA

The dysphasias (aphasias) are language disorders resulting from disease processes, injuries, or other involvements of the language areas of the cerebrum which affect the comprehension and use of the symbols of speech. Occasionally these involvements are congenital. More often they are acquired through trauma, embolism, brain tumor, encephalitis, meningitis, degenerative brain diseases, or similar pathologic processes. Frequently dysphasia is one of the sequelae of cerebral hemorrhage when the damage is in the left hemisphere—the hemisphere in which the dominant speech center is normally situated. At present, we are seeing a number of cases of dysphasia which resulted from head wounds sustained in the war.

Three types of dysphasia are usually distinguished: motor, sensory, and mixed. The patient with motor dysphasia, while understanding spoken language, has difficulty in expressing himself. He cannot evoke the right words or, in some cases, cannot evoke the memory of the coordinated movements necessary to produce them. He may be completely bereft of all speech, or he may simply be unable to recall certain words. Occasionally he has difficulty with certain types of words—verbs, for example—or with sentence construction. The patient with sensory aphasia suffers from a disturbance in the perception and understanding of spoken language. Usually he has an intact vocabulary, but a vocabulary whose meaning has been lost to him. Thus, although he usually is able to speak fluently, his conversation is a jargon. The patient with mixed dysphasia presents symptoms of both the motor and sensory types. The “pure” forms of the disorder are rare, the mixed type being most frequently encountered.



Group psychotherapy of stutterers.

Occasionally there is a spontaneous partial or complete recovery from the dysphasia as the acute stage of the pathologic process subsides. When there is no spontaneous recovery of the speech function, or when recovery is incomplete, speech reeducation is indicated. The aim of such reeducation is to build up a new set of associations between words and the ideas and objects for which they are symbols. Since the symptomatology of dysphasia varies, specific remedial procedures must be adapted to the individual case.

DYSPHONIA

The dysphonias, the last major category of speech and voice conditions, are defects or disorders of phonation. Perhaps the most prevalent of these disorders is trachyphonia, hoarseness, a condition which should never be dismissed lightly since it is often the first and only early symptom of cancer of the larynx.

Psychophonasthenia—One of the most interesting of the dysphonias is psychophonasthenia, a condition which develops in late adolescence or in adulthood and most frequently afflicts men and women in professional life. The voice is strained and tremulous and "cracks" frequently, sometimes choking off completely.

The disorder is often attributed to fatigue or voice strain and diagnosed as phonasthenia. The physician is often aided and abetted in making this diagnosis by the patient who, anxious to "legitimize" his disorder, will usually give a history of laryngitis, respiratory illness, or vocal strain in an effort to establish the organic plausibility of his symptom. However, the disorder is one of psychic origin—a symptom of neurotic anxiety that has been physiologized in the vocal tract—and for that reason I have termed it psychophonasthenia.

Psychophonasthenia appears to be the expression of a personality with a great deal of aggression that has been suppressed and has turned inward. Although usually above average in intelligence, the patient is emotionally immature and unstable and gives evidence of being extremely inhibited, tense, and anxious. The case history will usually reveal that these characteristics were well marked before the appearance of the voice disorder itself, suggesting that psychophonasthenia is the culmination of a neurosis which has been developing over a period of many years. Since the underlying conflicts are deep-rooted, treatment must usually be prolonged. Both group and individual psycho-

therapy are indicated, and it is often necessary also to introduce a certain amount of voice training in order to correct bad vocal habits resulting from the constant misuse of the laryngeal muscles.

Falsetto voice—Falsetto voice is another type of dysphonia which the physician occasionally encounters. It is an abnormally high, shrill voice in the male, and is occasionally associated with a glandular involvement, although this is less often so than is popularly supposed. In the majority of cases that I have seen, the voice disorder appears to have developed initially because of hypersensitivity during the pubescent period. The patient with a falsetto voice typically gives a history of having been a shy, sensitive, somewhat neurotic child. Such a child is more than ordinarily embarrassed by the somatic changes of pubescence, and especially by the voice change which gives to the world objective evidence of his approaching maturity. In his embarrassment and his state of uncertainty, he strives to cling to the security of childhood a little longer and unconsciously inhibits the voice change. Through continued misuse of the laryngeal muscles, the levators remain in dominance, keeping the larynx high in the neck, and the childish treble becomes a permanent feature. The condition, if uncorrected, continues throughout the individual's entire life; and since a certain stigma is attached to the disorder by virtue of the fact that a high, feminine voice is characteristic of the eunuch and eunuchoid, the man with a falsetto voice is usually subjected to many traumatizing experiences which increase his sensitivity and aggravate his neurotic tendencies.

Of course, in certain instances there is an endocrine involvement. In such cases the voice disorder is but one aspect of the whole symptom complex, and it is comparatively easy for the diagnostician to recognize the endocrine type merely by observation of the picture which the patient presents. He usually shows a quite apparent deviation from the so-called morphologic normal. For instance, he may present a picture of general under-development. On the

other hand, he may present the typical Fröhlich syndrome, with its characteristic female distribution of fat around the hips and breasts, large abdomen, and under-developed genitalia. Or he may be an elongated eunuchoid type; while such a patient is altogether different from the Fröhlich type, it is nevertheless readily apparent that he is atypical.

In general, prognosis is favorable in cases of falsetto voice. The larynx can usually be lowered through manipulation so that the depressor muscles assume dominance. This dominance must be reinforced by voice training, and a period of psychotherapy may be indicated as a supplementary measure. In those cases in which there is a glandular involvement, endocrine therapy may also be indicated.

Aphonia following laryngectomy—A number of voice disorders are due to iatrogenic defects—defects which result from measures instituted for therapeutic purposes. The most far-reaching in its influence on the voice and in its total effect on the patient is the extirpation of the larynx.

LARYNGECTOMY is usually performed, of course, because of cancer of the larynx. Since the larynx is an integral part of the respiratory apparatus, its extirpation removes a section of the normal air passage; thus the patient no longer breathes through his nose and mouth, but through the opening in his neck to which the trachea has been sutured. Laryngectomy thus robs the patient of the two essentials for producing voice in the normal manner: (1) a mechanism capable of vibrating (the vocal cords); and (2) a moving column of air flowing past the vibratory mechanism and through the mouth.

Fortunately, however, it is possible to teach a patient who has lost his larynx to develop a substitute voice by swallowing air into the esophagus and then slowly regurgitating it. Usually there is in the pharynx sufficient loose tissue to serve as a vibratory mechanism and thus to produce sound when air is expelled. The patient learns to articulate as he produces

the esophageal voice and gradually begins to talk again.

An esophageal voice is not as pleasant as a voice produced in the normal fashion, but it is adequate and enables the person to "carry on" socially and vocationally. To note the change in the patient's mental attitude and outlook on life when he finds it possible to speak again despite the loss of the larynx, is one of the major satisfactions to be derived from work in this complex field of speech and voice disorders.

CONCLUSION

In conclusion, I want to emphasize again the fact that speech and voice disorders seldom develop as isolated phenomena but, in the great majority of cases, are peripheral manifestations of some underlying psychic or somatic involvement. If the physician will keep this in mind, he will then ask himself, "What is the significance of this symptom?" The answer will often suggest the necessary therapeutic procedures.



Historical Epochs in Medicine: The first ovariectomy.

The Bettmann Archive.

Diseases of the Thyroid

GEORGE CRILE, Jr.

THE CLEVELAND CLINIC, CLEVELAND

FIVE YEARS ago thyroidectomy was accepted as the treatment of choice for hyperthyroidism. Today medical treatment with the recently developed anti-thyroid drugs can safely, completely, and in some cases perhaps permanently, control hyperthyroidism, and it is rapidly gaining favor as a definitive treatment for certain types of hyperthyroidism.

The controversy at the moment centers about what types of hyperthyroidism should be treated medically and what types surgically. It is much too early to draw final conclusions as to the long-range efficacy of the anti-thyroid drugs of the thiouracil series, and it would be unwise to attempt to make unqualified evaluations of definitive medical treatment. Nevertheless, it appears that thyroidectomy is no longer the treatment of choice for all diffuse goiters with hyperthyroidism. I am referring now to Graves' disease and am distinctly *not* referring to adenomatous goiter with hyperthyroidism or the so-called toxic adenoma. It is in Graves' disease, exophthalmic goiter, or diffuse goiter with hyperthyroidism, whichever you call it, that we now believe medical treatment is the initial treatment of choice, and we believe that in many cases hyperthyroidism can be controlled by the use of the new and relatively nontoxic propyl thiouracil with lower mortality, with less morbidity, and with greater economy than with thyroidectomy.

Thiouracil proved far too toxic for general use. The mortality associated with its use was comparable to that of thyroidectomy in good hands. This toxicity and the natural concern which was expressed by both doctor and patient while under treatment with thiouracil led to a prejudice against the anti-thyroid drugs, a prejudice which has been perhaps wrongly carried over and applied to the newer and less toxic drugs in this series.

Propyl thiouracil to date has proved both safe and effective. It is difficult to estimate how many patients throughout the country have been treated with this drug, but it must now be close to a thousand, and so far as is known at the present time there has been no mortality following its use. There has been only one reported case of agranulocytosis, and this, as I understand, occurred in a patient who had had two previous episodes of the same condition prior to the time she began to take the drug.

We have felt, in using propyl thiouracil, that its toxicity is sufficiently low that it is not necessary to do the weekly or bi-weekly white blood count or to keep the patients hospitalized or under close observation. We merely warn them to report at once any fever, dermatitis, or sore throat which they develop, or any feelings of malaise. We feel this is sufficient, and so far in over 120 patients definitively treated with propyl thiouracil we have had no cause for regret, because we have had only one patient who has developed even a granulopenia. I will present that patient a little later this morning.

persisted to the present, but two weeks ago she was started on iodine and I believe that we will find that that is now gone. These usually subside promptly when iodine is given.

She has gained 11 pounds; her pulse rate is 72; the eye signs have gone; the gland is now smaller, and she feels essentially well.

The question with this patient is, should we now subject her to thyroidectomy? My feeling is no, because she has at least a 50-50 chance at present of remaining well following withdrawal of the drug, so why operate on a disease which may already be cured? If she will continue to take the propyl thiouracil, which does not bother her at all, for another period of six months her chances of obtaining a longstanding remission are probably further increased. She has shown no toxic signs and there is no reason to believe that she will.

Mrs. H., would you come forward, please, to the microphone? I would like to ask you how you feel at the present time as compared with before your illness?

MRS. H.: I feel splendid.

DR. CRILE: I have gone through this with her several times in regard to her feelings before and after. As far as I can make out, neither Mrs. H. nor any patient who has diffuse goiter with hyperthyroidism completely controlled with propyl thiouracil has any residual symptoms referable to the disease.

Has there been any untoward effect of the medication? Have you felt sick in any way?

MRS. H.: None whatsoever.

DR. CRILE: Do you consider that taking the medicine is too much of a chore? Is it much trouble having your metabolism and your blood count checked regularly? Does it interfere with your daily life?

MRS. H.: Not at all.

DR. CRILE: She has been working right along throughout the treatment, and economically that is very important to some people. What would your reaction be at the present time to having a thyroidectomy?

MRS. H.: Well, I would rather take these little white pills the rest of my life.

DR. CRILE: That is the answer right there. The patient in the long run makes this decision. If you are honest with patients and tell them they can take this medication, which is, as far as we know, quite safe at least as compared with thyroidectomy, the rest of their lives if necessary, I am sure many of them will react exactly as Mrs. H. has.

If the hyperthyroidism recurred after the propyl thiouracil was discontinued a year or six months from now, you would not feel discouraged? Would you just as soon continue to take the medicine indefinitely?

MRS. H.: Absolutely.

DR. CRILE: Thank you. That is what I consider an ideal case not only in the type of hyperthyroidism but in the fact that we are dealing with an intelligent, cooperative patient who is, of course, in close contact with the medical profession. I believe that almost any of us would admit that when we have a medical means of controlling hyperthyroidism it is preferable in such a case.

THE SECOND patient I would like to present is Mrs. B., who had almost an identical history, a typical exophthalmic goiter coming on rather quickly. She had had iodine before we saw her. She is the only case in over a hundred patients whom we have treated with this drug who has shown any signs of toxicity and who has required a thyroidectomy. Mrs. B.'s basal metabolic rate was +45 per cent when she was first seen. Her basal metabolic rate fell to +19 on iodine. She was placed on propyl thiouracil and remained on the drug for about three months, but during that time she had frequent sore throats, which, by the way, were not associated with any leukopenia; she just seemed to develop one upper respiratory infection after another, and she was always worried about that because she had been warned about sore throats. Finally, after three months her leukocyte count did fall to around 4,200, and that was associated with only 25 per cent granulocytes. Her nervousness over the possibility of agranulocytosis, the fact that she had been so

slow in responding to the drug, and the undesirability of continuing to treat her over a long period of time with a drug to which she was showing toxic reactions, led us to go ahead and perform a subtotal thyroidectomy.

Mrs. B., I should like to have your reaction to how you felt while you were taking propyl thiouracil. Did you think there was any improvement in your general condition during the time you were taking it?

MRS. B.: None whatsoever.

DR. CRILE: I should also say that two of those months she was on the small dose originally recommended, which has subsequently proved to be insufficient—75 mg. a day. In the majority of cases, this dose is insufficient to produce a prompt subsidence of the symptoms, but even when Mrs. B. was on large doses she noticed no improvement.

How do you feel now?

MRS. B.: Wonderful.

DR. CRILE: This case is an argument for thyroidectomy, but the patient did not have a fair trial of propyl thiouracil because she did not take the drug long enough to make her metabolism fall to normal. Sooner or later, if we had been able to continue the drug without too much mental disturbance to both her and ourselves, she would have responded just as well to the use of the drug as she now has after subtotal thyroidectomy.

Thank you.

The next patient I would like to show had a nodular goiter with severe hyperthyroidism and complicating diseases. The problem in his case was the difficulty in obtaining his cooperation due to the fact that he understood English poorly and lived some distance away and it was inconvenient for him to come back and forth. He had a very severe hyperthyroidism, was very seriously ill and I feel certain could not have survived subtotal thyroidectomy with ordinary preparation with iodine. He was therefore prepared with propyl thiouracil and then subjected to thyroidectomy. He had a nodular goiter of the type which we still believe should be treated surgically.

He is 66 years old; he had lost 75 pounds of weight in two years, and in addition had epigastric pain and had been jaundiced for a month.

PHYSICAL examination showed auricular fibrillation, exophthalmos, a nodular goiter, weight loss, jaundice and the liver down two finger-breadths below the costal margin. The basal metabolic rate was +54. The electrocardiogram showed coronary disease.

The diagnoses in his case were nodular goiter with hyperthyroidism, auricular fibrillation, jaundice due either to cirrhosis of the liver or to hepatic damage from hyperthyroidism of long standing.

He was given 100 mg. of propyl thiouracil daily. At the end of two months his basal metabolic rate fell from +54 to +27, in three months to -4 per cent. He gained 10 pounds, the jaundice disappeared, the liver went back to normal size, and he was then subjected to a subtotal thyroidectomy.

His postoperative course on paper was smooth. The maximum temperature was 99.6 and the maximum pulse 100. In spite of that, in spite of the minimal postoperative reaction, with hyperthyroidism completely controlled, he was still so close to the borderline of overwhelming toxemia from long-standing hyperthyroidism and the liver damage that he was confused and delirious at night for a week following operation and gave us considerable care and anxiety.

He has now gained about 30 pounds and feels entirely well.

He says that he began to feel better about two months after he began to take the medicine. He felt definitely improved before the operation, but his metabolism had only been within normal limits for about three or four weeks before he was operated and he had not had time to obtain the full feeling of well being which one does obtain if the drug is continued for a long time, as was true in Mrs. H.'s case. He now feels entirely well.

You see how difficult it would be to handle

such a case indefinitely on propyl thiouracil when the language difficulty presents the problem of interpreting what is going on.

The final case is Mrs. T., who is 67 years of age and has a nodular goiter with severe hyperthyroidism and pernicious anemia and other complicating diseases. Because of her age and these complications, we have elected to treat her definitively with propyl thiouracil in spite of the fact that her goiter is a large, nodular, recurrent, intrathoracic goiter. She has no pressure symptoms and her age along with the other diseases make it seem advisable not to subject her to operation.

She had a thyroidectomy eleven years ago and a partial hemiplegia eight years ago. In the past six months she lost 37 pounds of weight and has had dyspnea, palpitation, nervousness and upper abdominal pain. She had a blood pressure of 240/110 and cardiac decompensation on entry. Her basal metabolic rate was +48 per cent and the blood, gastric analysis, and so forth, were consistent with pernicious anemia. Her electrocardiogram showed coronary disease.

Final diagnoses: recurrent intrathoracic goiter with hyperthyroidism, essential hypertension, hypertensive and hyperthyroid heart disease with decompensation, and pernicious anemia.

She was given 200 mg. of propyl thiouracil daily, liver extract and digitalis, and after four months of treatment her blood count is now normal, her heart is compensated, her pulse rate has fallen from 132 to 72, and she feels quite well. She has gained only eight pounds, but her metabolism has not fallen entirely to normal yet. This feeling of well being and the clinical improvement usually precede by a little the fall of the basal metabolic rate.

The question is, of course, should we advise operation. It is my feeling that if a patient such as this who has had a hemiplegia and severe hypertension and is 67 years of age has a goiter technically difficult to remove, she can better be carried along as she is on this relatively non-toxic drug.

How do you feel at the present time?

PATIENT: FINE.

DR. CRILE: You are able to do your work about the house and all of that without difficulty?

PATIENT: Yes.

DR. CRILE: Before that, she was incapacitated. You are willing to continue to take the medicine and you prefer that to operation?

PATIENT: Yes.

DR. CRILE: It doesn't require much care. She merely takes these pills, comes in every couple of months for a BMR checkup, and finds it no trouble.

In summary, I think we can safely say that since the risk of continuing to give propyl thiouracil for from six months to a year is so slight, it appears that in diffuse goiter with hyperthyroidism, medical treatment should first be given a fair trial and thyroidectomy advised only if the patient is intolerant of the drug, fails to co-operate, or for some reason prefers thyroidectomy. Such cases will, I believe, be few. In the past eight months I have had to operate on only one patient with Graves' disease.

One criticism of medical treatment of hyperthyroidism has been that it is possible that a carcinoma of the thyroid may be overlooked, but carcinoma of the thyroid does not occur in Graves' disease or in diffuse goiter with hyperthyroidism; it is in the nodular goiters that it occurs. At least if it does occur, it is so rare in diffuse goiter that I have not seen it. Even in nodular goiters the association of carcinoma and hyperthyroidism in the same gland is rare because it usually means that you have to have two separate adenomas in that gland, one which has developed a carcinoma and one which has developed a hyperfunctioning physiologic activity. It is extremely rare to have a carcinoma which itself hyperfunctions.

WHILE on the subject of carcinoma, I should like to present two patients who have had one of the more favorable types of thyroid carcinoma. These patients have papillary tumors of the thyroid with metastases to the lateral cervical region. It is a controversial point whether some of these papillary carcinomas of the thy-

roid with lateral cervical nodules represent multiple aberrant thyroid tumors of congenital origin, multiple primary tumors, or whether the lateral cervical nodules are actually metastases. In one of these patients, histologically the tumor was benign, although there were 20 to 30 lateral cervical nodules present. In the other patient, the tumor was histologically malignant, and in his case there was bilateral involvement with 20 or more nodules present on each side and in the superior mediastinum.

These patients were young when they came to us, 19 and 27 years of age, respectively. It is now five and nine years, respectively, since radical removal of the affected lobes of the thyroid and a dissection of the lateral cervical regions, and both continue well and their chest plates at the present time are normal.

EVEN in the presence of extensive lateral cervical tumors, prognosis may still be quite favorable in this type of thyroid carcinoma. I call it to your attention because if you think of this you will find a fair number of patients with this disease. They are not uncommon; we have seen 30 or 40 such patients in the last 10 to 15 years. You will find that they have a hard tumor in the thyroid gland, and in addition, have multiple nodules in the lateral cervical region. You may feel nodules under the sternomastoid in the neck—they may be high, they may be low. The commonest place is right under the sternomastoid. One of the things they are most frequently mistaken for is tuberculous glands of the neck. Always examine the thyroid carefully, have the patient swallow, and if you feel a little firm nodule in the thyroid, the chances are that you are dealing with one of these papillary carcinomas of the thyroid with lateral cervical metastases or multiple primary lateral aberrant tumors, whichever you call them.

The reason this group is of particular significance is that it represents the most favorable type of thyroid carcinoma from the standpoint of cure. It makes little difference if you can recognize a carcinoma which you cannot cure, the ultimate outcome is the same; but here you

are dealing with a type of carcinoma which is curable if an adequate operation is performed.

Interestingly enough, it does not require a block dissection of the neck. We have now operated on some 25 patients whom we have had opportunity to follow for over five years and none of these have had block dissections of the neck with radical removal of the sternomastoid, jugular vein, and so forth. They have merely had a careful dissection, with removal of the glands, and in no case has there been uncontrollable recurrence of lateral cervical nodules. In only one case has there been distant metastasis through the blood stream.

This is the woman I told you about who had over 20 lateral cervical nodules scattered all the way from the superior mediastinum, with some below the clavicle, to just under the mastoid process with involvement of the right lobe of the thyroid as well.

The incision we used was a lateral cervical incision, which as a rule in mature adults heals very well, and the cosmetic appearance is good. In children it may cause a keloid. She does not have the deformity associated with ordinary block dissection of the neck. That is an important thing, because most of these tumors occur in women and most of them occur in young women, and you do not like, if you can possibly avoid it, to produce a deformity of the neck when equally good results can be obtained by a more conservative procedure.

She has been well ever since, with the exception of a nodule which occurred right in the midline, completely out of the field of operation, but present from the time of operation. This was an overlooked nodule which was removed sometime later, and that is the only residual that she has had. She is now well and the x-ray of her chest is negative.

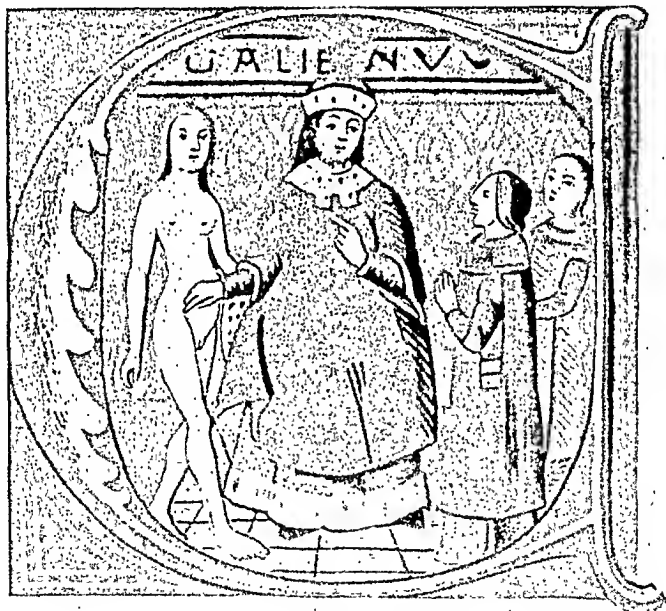
Mr. G. had the same thing, except in his case it was bilateral, with both sides of the neck involved, and he had a bilateral neck dissection. He had at least 25 nodules on each side scattered throughout the entire cervical region. The entire lobe on the left was removed and on the right all of the thyroid was taken except for a

tiny shell containing a parathyroid. He also had mediastinal nodules. These things tend to go into the mediastinum and posterior to the carotid sheath, all the way into the posterior cervical region, up to the level of the mastoid process sometimes. It is the most extensive one we have seen, and yet Mr. G. has now been entirely well for five years and his x-rays show no evidence of metastasis.

IN SUMMARY I think we can say we must give serious consideration to medical treatment

for diffuse goiter with hyperthyroidism.

If we are to reduce the mortality rate from carcinoma of the thyroid, it will not be by observing adenomas until we can make the diagnosis of carcinoma, because when you can make that diagnosis clinically it is too late in the majority of cases to establish a definitive cure. It is only by prophylactically removing any suspicious adenoma of the thyroid that one can hope in the long run to reduce the mortality rate from carcinoma.



The Edinburgh Archives

Historical Epochs in Medicine: Galen, Prince of Physicians, (ca. 130-200 A. D.) is shown in this medieval miniature lecturing on gynecology.

DIAGNOSTIC CLINIC

Treatment of Syphilis with Penicillin

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THE USE of penicillin in the treatment of syphilis has been one of the greatest advances made in handling syphilis since man has been fighting this plague. We can all remember when we were forced to depend only on arsenical therapy and bismuth therapy. Any of us who have used this form of therapy can remember the many anxious moments we had in connection with arsenical reactions and arsenical deaths.

Later, Wagner-von Jauregg in Vienna suggested the use of fever treatment in central nervous system syphilis. Then Kyrle, also of Vienna, showed that the use of fever alone was not applicable to early syphilis.

It was next suggested that the arsenical injections be given more frequently; instead of giving only two or three, they began giving them once a week, then even twice a week, and later started the use of the intravenous drip. There is no question that a very appreciable proportion of the patients were cured. On the other hand, the reactions that ensued from this form of therapy were terrific. It appeared that further search was necessary.

A method was tried using an injection of an arsenical once a day for ten days, with bismuth about four times during that period of therapy, and with fever treatment on the second, fourth, sixth, and eighth days. This was the Thomas

method of treatment from which we had good results, but also some severe reactions. This led up to the Army treatment suggested in the early part of the war: 40 injections of an arsenical and 16 injections of a bismuth compound in a twenty-six-week period.

Penicillin, the new remedy, then became known. When penicillin was found to be effective in the treatment of many infections, notably pneumonia, it was only natural to see what the new drug would do in the treatment of syphilis. Several workers tried its effects in experimental syphilis in rabbits. For some reason—we do not know just why—their experiments were not successful. Then John Mahoney and collaborators at the United States Public Health Service at Staten Island did some work with experimental syphilis in rabbits; later they reported on four patients with acute syphilis to whom they had given 2,400,000 units, giving it every three hours over a period of fifteen days. They still have two of these patients under observation and they are well.

It was around this time that the war started. Since syphilis is one of the scourges of war, the Army, the Navy, the Public Health Service, and the National Research Council, through the Office of Scientific Research and Development, launched one of the most gigantic cooperative medical investigations that has thus far been conducted on a public health problem. More has been done under this cooperative program in three years than was done in the preceding thirty years.

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Presented before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio, October 15 to 18, 1946.

Much of the credit for this is due Professor A. N. Richards of the University of Pennsylvania, chairman of the Office of Scientific Research and Development committee; to the Committee on Chemotherapy of the National Research Council headed by Chester Keefer of Boston, and to the Penicillin Panel that was established to supervise and carry on the work. The Penicillin Panel, under Earl Moore of Baltimore, consists of syphilis clinics in various parts of the country, many of them operating in connection with universities like those at the University Hospital and at the Cleveland City Hospital, which are associated with Western Reserve Medical School.

We also must give credit to Surgeon General Thomas Parran of the Public Health Service, who has taken over this project since the Office of Scientific Research and Development has been dissolved.

What are the results of this work to date? I should like first to say just a word about the routes by which penicillin is used. At present, penicillin should not be given by mouth or by the rectal route. The dosage is too inexact.

Intrathecal use of penicillin is not without danger and should not be employed.

The intravenous method of treatment may be used, but is not applicable either for the physician or for the patients.

The intramuscular route is the preferable route thus far, the injections being given often enough to get and keep a high level of penicillin in the blood stream. Trouble results from varying levels of penicillin in the blood stream; for best results, a high level must be kept more or less continuously in the blood stream.

Another method of therapy has been suggested by Romansky of the Public Health Service—the use of calcium penicillin in peanut oil and beeswax. I mention this but I do not recommend it for the regulation treatment of acute syphilis. As a general rule, the preferable method is the use of the intramuscular injection every two to three hours, day and night, for seven and a half to fifteen days, depending on the duration of the infection.

I think we are all acquainted with the results that are achieved with this form of therapy.

WE PRESENT here a patient who is in the early stage of syphilis. He has contracted a primary lesion and has developed an extensive generalized annular papular eruption over his body and has been under therapy with penicillin for seven and a half days. His eruption has practically cleared up. Ordinarily, in an individual with an early infection, we find that the organisms disappear from the primary lesion in a matter of hours, seven to eight or ten or twelve hours at the most. The generalized eruption, depending on its severity, will clear up in a week to two or three weeks.

Probably the most important factor in controlling these cases is the titrated serologic examinations of the blood. It is not enough simply to say that the patient has a 4+ reaction or a 3+ reaction. It is necessary to have the patient's blood tested and titrated every month. It is not necessarily the number of units that has the most significance, because 8 Kahn units and 84 Kahn units will still be strongly positive reactions. It is the trend of the titer that counts, and by taking a titrated specimen once a month and examining it, you will be able to get some idea of how the patient is responding to treatment.

This patient had 64 Kahn units in his blood stream when he came to the clinic. He will be observed every month. If his titration goes up a few units in the beginning after the treatment, as is so often the case, we will not be alarmed; maybe the next month it will begin to drop; perhaps the next month it may even go up a little bit and then begin to drop. I repeat that it is the titrated curve that counts, and what we desire is a curve trend that will gradually drop to the base line, zero, and remain there. The patient is not considered cured until this has gone on for one year with completely negative serologic reactions. Any physician who treats syphilis with penicillin is not doing his duty by his patient unless he uses titrated tests.

In early syphilis, the best results will be

achieved in the so-called seronegative primary phase where diagnosis is made with the darkfield and treatment is started before the serologic test has become positive. In such patients it would be well to give, over a seven and a half-day period, 3,600,000 units of penicillin, giving the injections every three hours day and night. If the process has lasted for a somewhat longer period of time, it probably would be well to give 5,400,000 units over about the same period of time.

An editorial about penicillin entitled "Facts and Rumors," in the *Journal of the American Medical Association* some time ago, pointed out that we first used a crude penicillin; that later it had been perfected; and that whereas in the beginning there were not many units of penicillin per milligram, this had been increased; also that most penicillin consisted of F, G, X, and K. At present most of the penicillin on the market is G; there may be a certain amount of the other components. Unfortunately, in 1945 there was quite a lot of penicillin on the market that had K in it. K is very rapidly destroyed and is not the desired therapeutic type of penicillin. As a result, there were many relapses and the results of the treatment were not very good. At present, all penicillin is being very carefully observed by the United States Food and Drug Administration and by the Council on Pharmacy and Chemistry of the American Medical Association, so one need not hesitate to employ it.

How would you use penicillin in late and latent syphilis? In such situations, we have a process that has lasted for quite a period of time. In latent syphilis there will be no evidence other than a positive serologic test and a history of syphilis. In late syphilis, there are cutaneous tertiary lesions, gummata in the liver, and so on. For these patients, it is probably best to give a preliminary series of 6 injections of intramuscular bismuth, bismuth subsalicylate 1 cc., about once in five days, and then to put the patient on penicillin, about 3,600,000 units over a period of seven and a half to fifteen days. The preliminary use of bismuth



Harold N. Cole

is to obviate any therapeutic paradox; that is, too rapid healing of a lesion and perhaps the formation of scars and contractures that might be deleterious to the patient.

What are the results in central nervous system syphilis? We are all interested in that, because undoubtedly many of us have these types of cases.

RESULTS vary in central nervous system syphilis, depending upon the duration of the process and on whether the type of involvement is of the meningeal or of the parenchymatous type, such as we find in tabes and paresis.

When we first began the use of penicillin, we had a female patient 38 years old at the City Hospital who was given 300,000 units. That dosage today would, of course, bring a smile and that is about all; it was an absurdly low dose to employ. About a year later this patient, who had been under observation, came back to the clinic complaining of frontal headache, of confusion, of stiff neck. She had a paralysis of the left facial, and a paralysis of the left hypoglossal; a titrated blood specimen

showed 64 Kahn units. A lumbar puncture was done and it was found that she had 3,200 cells, mononuclears. In other words, she had a syphilitic meningitis. Her total protein was 65 mg. per cent, the normal being around 25 to, at most, 35 mg. per cent. She had a paretic curve, a serology in the spinal fluid that was strongly positive even with 0.1 cc. of the fluid. We titrate the spinal fluid also.

This patient was put on 4,000,000 units of penicillin. I will not mention the intermediate steps, but at the end of nine months her cell count on the spinal fluid was 10, which is the upper limits of normal; her total proteins were 20 mg. per cent; her gold colloid curve was completely flat, changing from a paretic type; she still had a 3+ reaction with 1 cc. only of the spinal fluid. In her blood serologic tests, the titer gradually has dropped and has become completely negative.

We felt this patient was cured. She has been kept under observation since then. We have continued to do titrated serologic blood tests on her, also lumbar punctures, and thus far we have found no reason to give her further therapy.

That indicates what may occur if you get a case early and put it under proper therapy. These patients must be carefully followed, however. The older the involvement of the central nervous system, the poorer the prognosis. This is particularly true with parenchymatous involvement such as we have in tabes and in paresis.

This patient is an indication of the necessity of early lumbar punctures on all cases of syphilis. They should be followed along, and while under observation and treatment should have a lumbar puncture certainly every six months, if negative, and every three months, if positive. Only in that way can we be sure to detect an early involvement of the central nervous system and start treatment.

ONE of the places in which we get a brilliant result in syphilis is in pregnancy. In our clinic we have treated 1,500 or 1,600 cases of various forms of syphilis with penicillin, and we

have had about 65 cases of early syphilis in pregnancy. Some of these mothers have even had a second child and in a couple of instances have had twins.

We have had but two cases of congenital syphilis in the entire group where penicillin has been employed. That is a real achievement in medicine. In these two cases, as you will see, it was quite excusable that this should occur. In one instance the mother had one of the low dosages, 300,000 units, and she, of course, had a relapse. The child was born with a mucocutaneous syphiloderm and a meningitis. The child was put on treatment and is well today. In the other case, the mother came into the City Hospital with a generalized syphiloderm. We managed to give her two days of penicillin therapy before the child was born. Naturally, that was not sufficient and the child had a syphilitic meningitis, a generalized eruption, and the typical changes that are found in the bones in congenital syphilis.

We have had eleven different mothers who received treatment in the last three to four weeks before their babies were born, another one week before, another five days before, and three just before and during the pregnancy so that we were not able to give all the penicillin before the child was born; yet all the children are well today.

It is necessary to do a titrated Wassermann on these children. We do it every month. You get the cord blood Wassermann test, which, of course, is the mirror of the mother's situation. If the titer drops, it indicates that the child has been cured. After observing the child for a year we feel that he is well. If, on the other hand, the titer goes up, we look for a relapse and, after consideration of the radiographic studies, may decide to put the child on treatment.

One patient we had under treatment is 19 years old; she had a generalized eruption of syphilis for one month before she came into the hospital; she is in the fifth month of pregnancy and has been placed on penicillin. It is probably just as well to start these pregnant mothers with small doses at first. She was put

on 20,000 units every three hours for eight doses and then 80,000 units every three hours for 118 doses. She has cleared up and we expect to get a perfectly normal child in this case and hope the mother will be cured.

In congenital syphilis, penicillin is again of great value. We may have to use supportive measures for a few days, such as bismuth, and then put such patients on penicillin therapy, giving 100,000 to 400,000 units per 2.2 pounds, that is per kilo, over seven and a half days. These patients, of course, must also have a titred serology.

We now come to another problem in connection with syphilis, the subject of relapse, a very important aspect of the disease. There are different types of relapse, as we may imagine.

For instance, one patient, a woman 36 years old, received 1,600,000 units of penicillin in October, 1945. The titer was 32 Kahn units. With this therapy the titer gradually dropped to 4 Kahn units. It never went down to the base line. We followed it along, and all at once it rose to 32 units. The patient was hospitalized. There were a few mucus patches, indicating that the patient was just relapsing. She has been put on therapy again and we are confident that she will respond to a higher dosage—9,000,000 units.

We are seeing quite a few examples of relapse in individuals who have had Neisserian infections and have had a single injection of penicillin calcium in peanut oil and beeswax. The doctor does not detect the primary in-

vasion of syphilis. Perhaps nothing shows at the time and unless these patients are followed monthly with a titrated serology for four or five months, the physician may overlook a syphilitic infection that took place at the same time as the Neisserian infection. It is very important in all cases with Neisserian infection treated with a single injection of penicillin calcium in peanut oil and beeswax that a titrated serologic test of the blood be taken monthly.

I THINK there is no question but that we have a very valuable remedy in penicillin. One reason is that there are no severe reactions with it. Rarely is there an angioneurotic edema, for example, or a dermatitis exfoliativa. We do not have to worry, as was formerly the case with arsenical therapy. That in itself will be a great help. Moreover, we have a remedy that renders the patient innocuous as far as public health is concerned in at least two weeks. Also, we have a remedy we have never had before for treating syphilis in pregnancy and for treating congenital syphilis. And, too, this probably is going to offer us far more than we have had before in the treatment of central nervous system syphilis. While we are going to find that it will be elaborated a great deal over what we now have, and better methods of administering it may be brought out, even today considering the absence of severe reactions we have a remedy for treating syphilis that is better than anything used in the past.

EDITORIALS

INTER PRIMA

THE BIRTH and development into full maturity of the present Interstate Postgraduate Assembly is a story in itself. In its conception a need was visualized and in its growth a true service has been performed. As an organization, it has weathered war and peace, criticism and praise, depression and prosperity and is bigger and better for all of these experiences.

Motivated primarily by the ideal of service to the medical profession and through it to humanity, it is natural that all means of furthering this end be considered. Among the ideas mulled over for years has been that of sponsoring a medical journal. For one reason or another not until now has the idea been translated into reality.

There are those who are of the opinion that there are already too many medical journals and magazines. There is much to be said in support of this opinion. It is equally true that there are not too many in the top bracket.

It is and will be the objective of those concerned with *Postgraduate Medicine* to produce an authoritative, diversified, stimulating medical journal of which American medicine will be proud.

C. W. M.

POSTGRADUATE MEDICINE

*Official Journal of the
Interstate Postgraduate Medical Association*

Editor in Chief

CHARLES W. MAYO

Managing Editor

ARTHUR G. SULLIVAN

Assistant Editor

SYLVIA S. COVET

JANUARY, 1947

EPITOME OF MEDICAL KNOWLEDGE

THIS journal is published with the object of giving progressive medical men an epitome of medical knowledge and teaching on matters of practical importance in their daily lives. We will present authoritative original articles of high scientific value and great clinical interest. The emphasis will be on treatment. The approach will be informal. Medicine will be written about as it is found in actual practice rather than discussed as if it were on "dress parade." The basic editorial fare will be the seventy or more papers read at the annual meeting of the Interstate Postgraduate Medical Association assembly. The articles will be presented from the "doctor-to-doctor" point of view, in the

spirit of colleagues. The "teacher-pupil" manner will be taboo.

These pages should stimulate those whose interest lies in the furtherance of their knowledge for the benefit of their patients, and those whose ego feels the urge for profound thought. The discussions of selected subjects will be of utmost value in the collation of all recent knowledge on that subject and should prove of great value to physicians studying for higher qualifications.

Postgraduate Medicine will reflect the personality of its sponsor, the Interstate Postgraduate Medical Association. The general tone will always be clinical, the presentation practical. It was the very utility of the Postgraduate assemblies that caused the association, organized at a district assemblage of physicians in 1916, to expand successively to state, national and international levels. This same practicality will be preserved in the magazine, thereby increasing the scope of the association's postgraduate medical educational activities.

Beginning in 1925, the clinics and addresses presented at the Assembly that year were published in a single volume—the advent of the first of twenty issues of the annual Proceedings. In 1945, the United States government's ban on large assemblages prevented the holding of the 30th annual Assembly and caused a lapse in the publication of the Proceedings. Much thought was directed to the preservation and dissemination of the top quality contemporary medical instruction presented at each assembly. Despite rapidly rising publication costs and the diminution of subscriptions occasioned by the tremendous dislocation of doctors due to the war, the assembly decided to increase the selling price of the Proceedings, so that the income means of a

monthly magazine would afford the desired ends.

Establishment of a periodical not only would give a larger outlet to the Proceedings but also would permit the utilization of much splendid additional material. There was, though, a consideration not to be tossed lightly aside. Many physicians, clinics, medical school and medical society libraries had purchased annually and preserved all the twenty volumes produced since 1925. They might regret a change in publication policy. It has been heartening, indeed, to find that assurance of the continuation of the Proceedings in this new form has proved entirely acceptable to this group.

Freed from the strict spatial and cost limitations imposed on the annual Proceedings, *Postgraduate Medicine* will be able to publish much material which could not be presented at the assembly because of full programs. Since a good illustration is often worth a thousand words, the editorial policy of the monthly journal will be to use illustrations more lavishly than ever has been attempted by any other regular medical publication.

Supplemental features are being planned for the journal, several of which are included in this first issue. These departments are addressed to the doctor as a man, as well as a scientist. In this very space each month will be found editorials written by members of the editorial board or by contributors on topics related to the professional and scientific interests of medicine. Excerpts from outstanding editorials of other medical journals will appear each month in a department entitled "What Other Editors Think."

A Consultation Service is being inaugurated in which men may seek answers to the various problems that come up in their practice. "This Month in Medicine" will comprise a readable

summary of medical progress. Another department will be concerned with the activities of the Interstate Postgraduate Medical Association affairs. A Correspondence Column will give the reader the floor. Contributions, criticisms, suggestions and even diatribes will be accepted from responsible sources. The free and open nature of this department will serve as a safety valve on the editorial policy of the periodical and will be an assurance that the publication will be tolerant, open-minded, scientific and fair in its approach to all opinions on medical topics. The informality of the periodical itself will permit the printing of more vigorous letters than are usually to be found in a medical publication.

Fine writers and great reporters will be solicited for contributions to our "Men of Medicine" department. Literary quality as well as textual interest also will be emphasized in informal columns, such as "The Doctor in Literature." A book review department is being readied for introduction in an early issue. Other departments being considered include descriptions of new drugs and instruments and an authoritative section on clinical photography.

Thus our aims are high, our plans great. To achieve them the editors invite your urgent and express cooperation. Send in your papers and reports on your work, on your interesting cases. Send in your criticisms, adverse or laudatory, of the papers published in these pages. We shall not be afraid to print or publish all that is worthy of Medicine Today. Our editorial motto may well be borrowed from Matthew Arnold: "I am bound by my own definition of criticism; a disinterested endeavor to learn and propagate the best that is known and thought in the world."

And so at long last, in its 32nd year of teaching, the Interstate Postgraduate Medical

Association presents its official monthly publication, *Postgraduate Medicine*. J. G. C.

MAJOR, RENEW YOUR MALPRACTICE INSURANCE

MANY returned medical war veterans have failed to renew their protective policies. Malpractice suits are gradually again increasing in number. The curve in these law suits closely approximates the curve in the national "take home" income—with most claims being filed during the depressions.

A recent judgment assessed against an uninsured veteran who resumed his practice last April will keep him impoverished for a long time. He intended to renew his policy, lapsed during his service with the armed forces, but forgot the matter until the summons and complaint were served. A. G. S.

IS THERE AN "HYSTERECTOMY RACKET"?

A RECENT visit with a seasoned pathologist from a three hundred bed hospital disclosed his conviction that far too many uteri were removed than could be justified on the basis of the tissue examinations, or even by his personal review of the hospital histories of those patients. He pointed to the recent era when appendectomies, Caesarian sections, kinked ureter cases, and even blood transfusions reached such astronomical statistical percentages in many hospitals throughout the land—and not those exclusively treating charity cases. A nasty implication.

Legislation often has been proposed placing the legal burden of justification on the surgeon who removes an appendix which from the pathologist's examination was normal. Defeat of these proposed laws was largely due to the determination of the legislators that their own

normal appendices should be removed by their trusted surgical attendant if in his judgment, during an abdominal operation for other pathology, he decided that it was a prudent act of generosity to extirpate, in addition, this treacherous appendage.

Nevertheless, the hospital pathologists see a startling discrepancy in the number of hysterectomies done by surgeons with comparatively similar practices.

This coupled with the absence of supportive gross or microscopical pathological data assuredly poses the question—Is there an “hysterectomy racket”?
A. G. S.

SPECIAL TRIBUTE TO OUR EXHIBITORS

WE WOULD be remiss in this first issue, which now permits release from our former inarticulate status, if we failed to pay a richly-deserved tribute to the medical and the surgical manufacturers for the generous and loyal support which they have increasingly extended to the Interstate Postgraduate Medical Association at each annual meeting. Perhaps the most important factor in our success and progress has been the constancy of this generous support.

Aside from the monetary considerations, the exhibitors have brought to each Assembly a massive educational opportunity which observant and appreciative physicians have often remarked as being as interesting and valuable as the lecture courses themselves.

Far too few doctors appreciate the wealth of dependable information which may be obtained from our Exhibitors. Few realize that many of these men who patiently and repeatedly demonstrate the drugs, instruments, and appliances at our Assemblies, often are distinguished scientists.

How impotent we would be in our daily ministry to the sick if we had to compound our own unreliable remedies, or painfully fabricate our own tools, as once prevailed.

From the standpoints of both volume and mass accomplishment, it is a long time since bacteriological, pharmaceutical, physiological, and pathological research in this country passed from the medical schools and clinical laboratories to the increasingly expensive and productive research laboratories of the American medical and surgical manufacturers. The large medical schools and the great clinics of this country annually encounter, with painful regret, the transfer from their staffs of some of their most brilliant research workers to these tremendous research enterprises. Fortunate for both doctors and patients that manufacturers seek and can afford the best!

Detailing of drugs, instruments, and appliances to the doctors at medical meetings is at best an exhausting endeavor. It is innervating when the doctor is truly interested in the product demonstrated, and the more so, when the doctor's interest is enhanced by a background of competent education in the special field under consideration. It is wearying and painful when the doctor is an obnoxious individual with a superiority complex and devoid of any special information or training in the field discussed.

For the generous contribution made by the one hundred seventy-eight exhibiting firms at our recent Cleveland Assembly, we express our deep gratitude—and our readers will more fully understand when we acknowledge that the registration fees paid by the physicians present were sufficient to meet but twenty-five per cent of the costs.

A. G. S.

This Month in Medicine

CANCER RESEARCH

CANCER has increased in importance, as the population has aged. Indeed, during the past few years, perhaps no pathological condition has attracted more attention than has carcinoma. Numerous causes have been postulated; as many cures have been recommended. While much of this endeavor has led to naught, some suggestions have been peculiarly interesting and stimulating. The recent work of Ayre and his associates in Montreal is illustrative. These workers have followed the lead of Papanicolaou, in investigating the possible diagnosis of cancer by the vaginal and cervical smear techniques. Ayre extended the field, however, in describing a precancerous condition which is readily recognizable in smears, although the patient's cervix may show no objective evidence of disease other than a tiny circular reddened area about the external os. The smear reveals anaplastic squamous cells; abnormally high cornification; a tendency to multinucleation of the cornified cells; and atypical cornified cells showing large pyknotic dense nuclei. This association of cytological findings has been found to be indicative of precancerous squamous hyperplasia at the squamocolumnar junction.

Some months ago, Ayre and Bauld reported the association of an abnormally high endogenous estrogen level, a low thiamine excretion, and the presence of uterine cancer; now they find the precancerous cytological condition, the atypical hyperplastic and anaplastic cells, in individuals manifesting these high estrogen and low thiamine levels. Almost 90 per cent of 50 cancer patients showed this linkage, whereas the majority of a similar group of 50 normal individuals of the same age did not. Ayre suggests that some metabolic growth factor is involved, which is influenced by nutritional levels and is associated with estrogenic factors.

The findings of Ayre and Bauld could be interpreted in the light of Biskind's demonstration, that members of the vitamin B complex are essential

to the protection of the liver from toxic agents. With vitamin B deficiency, the liver cannot inactivate endogenous estrogen. Biskind's views fit nicely with the findings of Ayre and Bauld. Just why an excess of estrogen should cause uterine cancer is inexplicable, but over a decade ago Allen warned against the use of excessive estrogen therapy, on the grounds that it might stimulate neoplasms. In like vein, Henry, only last year, attributed two cases of precancerous or cancerous changes in the endometrium, to estrogen therapy.

Suggested Reading:

Ayre, J. E. (1946), Vaginal Cell Examination as a Routine in Diagnosis, *South. Med. J.*, 39:847, November.

Ayre, J. E.; and Bauld, W. A. G. (1946), Thiamine Deficiency and High Estrogen Findings in Uterine Cancer and in Menorrhagia, *Science*, 103:441, April 12.

Several papers by Biskind and his associates have appeared in *Endocrinology*, 30:819, May, 1942; *Gynec., & Obstet.*, 78:49, Jan., 1944; and *Exp. Med. & Surg.*, 3:299, Nov., 1945.

Henry, J. S. (1945), The Avoidance of Untoward Effects of Oestrogenic Therapy in the Menopause, *Canad. Med. Assn. J.*, 53:331, July.

CIRRHOSIS OF LIVER AND DIET

THE past month another paper appeared which touches upon a topic about which ideas are changing. For a long time cirrhosis of the liver has been associated with alcoholism. The association was fortuitous and based only on circumstantial evidence. And in spite of much data to the contrary, the habit of thought—alcoholism and cirrhosis—still persists. The more enlightened view, however, dictates that hepatic cirrhosis is primarily a nutritional disease and develops in an alcoholic who refuses an adequate diet. Hence the dietary treatment of cirrhosis, developed by Patek, Morrison, and others, has been endowed with a good measure of success. Meienberg and Snell studied 50 repatriated prisoners of war, who had for many months been given a deficient diet, but who had not had access to hepatotoxic agents, such as alcohol. Nor did they show evidence of systemic disease. A high incidence of hepatic damage was revealed among these men. In some only slight functional impair-

ment was noted, while in others the damage had proceeded to early cirrhosis. In the absence of other agents which could have been responsible, the authors reasonably conclude that dietary deficiencies produced the hepatic changes.

Suggested Reading:

Papers by Patek may be found in *Proc. Soc. Exp. Biol. & Med.*, 37:329, 1937; *J. Clin. Invest.*, 20:481, Sept., 1941; and *Bull. N. Y. Acad. Med.*, 19:498, July, 1943.

Morrison, L. M. (1946), The Response of Cirrhosis of the Liver to an Intensive Combined Therapy, *Ann. Int. Med.*, 24:465, March 1.

Meienberg, L. J., and Snell, A. M. (1946), Nutritional Deficiency as a Probable Cause of Hepatic Damage in Repatriated Prisoners of War, *Gastroenterology*, 7:430, October.

MAN AND MOSQUITOES

MELLANBY, in *Nature*, recently discussed a little-investigated field, the reactions of human beings to the bites of mosquitoes. He confirmed the views of others, that individuals differ widely in their reactions to insect bites, and that continued exposure may alter individual reactions. Mellanby divided reactions of human volunteers who had never been bitten by mosquitoes into four categories: (1) When a subject was bitten by *Aedes aegypti* for the first time, there was little cutaneous response other than a tiny red spot at the site of the bite, but 20-24 hours later a delayed reaction occurred, a red patch 3 cm. in diameter surrounding the bite, with a definite weal in the center, which persisted for several days. (2) After the individual had been bitten on several occasions for about a month, his cutaneous reactions were decidedly different. Immediately after a bite, a weal developed at the site of inoculation, an area of erythema surrounded the bite, and itching was intense. These symptoms disappeared within 2 hours, but 20-24 hours later the same delayed reaction occurred. (3) After many bites, over a longer period, reactions were again changed. The immediate reaction persisted, but the delayed reaction gradually became less severe and eventually disappeared. (4) Mellanby's subjects never showed reactions less severe than class 3, but in individuals who have been exposed to thousands of bites the immediate reaction is quite transitory and disappears almost immediately.

Human reactions show a high measure of species

specificity; thus a man may give a stage 1 reaction to *Aedes* and a stage 2 reaction to *Anopheles*. The whole problem, then, appears to be related to the antigens with which the mosquitoes, while feeding, inoculate human beings. Similar phenomena have been observed on the West Coast, where the native population is fairly immune to the bite of fleas, but newcomers are plagued with them. Investigations have been in progress for some years leading to the development of artificial antigens which, upon inoculation, render one insensible to the outrages of insects. Certainly such a product would be a godsend to those of us who are regarded as delicacies by the insect world.

Suggested Reading:

Mellanby, K. (1946), Man's Reaction to Mosquito Bites, *Nature*, 158:554, October 19.

STREPTOMYCIN EFFECTIVE IN SYPHILIS TREATMENT

THERE will probably never be too many cures for syphilis, because in any group of syphilitic patients there are refractory cases. Of interest, therefore, is the recent report of Johnson and Adcock that streptomycin effected a cure of syphilis in rabbits. These workers administered streptomycin to syphilitic rabbits at the rate of 42.5-45.5 mg. per kg. body weight per day. After 72 hours' treatment, spirochetes disappeared from material examined by darkfield; when the rabbit's testicles were transferred to two other rabbits, syphilitic changes did not appear. Other evidences of the effectiveness of the drug were manifest; popliteal transfers did not cause syphilis; the quantitative Kahn became negative.

Herrell and Nichols, some months previously, reported early favorable response to streptomycin in the treatment of human syphilis, but later relapses. The present authors point out that on the basis of body weight, their rabbits received 3-5 times as much streptomycin as did the human patients. The present work on experimental animals corroborates the findings of Dunham and Rake, who reported similar results. In view of these findings, further investigation of the anti-syphilitic activity of this interesting antibiotic are indicated.

Suggested Reading:

Johnson, S. A. M., and Adcock, J. D. (1946). Treatment of Experimental Syphilis in Rabbits with Streptomycin, *Proc. Soc. Exp. Biol. & Med.*, 62:109, June.

Herrell, W. E., and Nichols, D. R. (1945). The Clinical Use of Streptomycin, *Proc. St. Meet., Mayo Clinic*, 20:449, November 28.

Dunham, W. B., and Rake, G. (1946). The Activity of Streptomycin in Experimental Syphilis, *Science*, 103:365, March 22.

USE OF THIOURACIL IN HYPERTHYROIDISM

SINCE 1943, the medical treatment of hyperthyroidism has undergone a most radical change. The inhibition of thyroid endocrine function by thiouracil and thiourea presents a therapeutic mechanism which is novel to medicine. The indications and limitations of these drugs have been extensively explored, with the result that they may now be employed with assurance. Of late, a spate of papers have appeared which further define the conditions under which they, particularly thiouracil, the more active of the two drugs, may be used. Most authors believe that thiouracil should be used primarily as a preoperative treatment of hyperthyroidism. Means finds thiouracil, in combination with iodine, the most complete preparation that has ever been available for thyroidectomy. Egan believes that the prolonged use of thiouracil might be considered, if surgery is regarded as exceptionally hazardous. That is, he evaluates the hazards of medication against those of surgery. This view is shared by Haines and others. Fowler reports that serious toxic reactions occurred in not over 4 per cent of 1,573 hyperthyroid patients treated with thiouracil. To prevent granulocytopenia and other side effects of medication, Markson administered liver orally with the thiouracil. Although it did not prevent the thiouracil-induced granulocytopenia, it did apparently lessen the milder thiouracil side effects. Cavanaugh and De Courey believe that thiouracil should be used principally in those patients that have become "iodine-fast," or in those in which thyroidectomy is contraindicated.

Suggested Reading:

Means, *Ann. Int. Med.*, 35:403, Sept., 1946.

Egan, *J. Lancet*, 66:326, October, 1946.

Haines et al., *Med. Clin. N. Amer.*, 30:535, July, 1946.

Fowler, E. F. (1946). Treatment of Hyperthyroidism with Thiouracil, with Particular Reference to Toxic Reactions, *Int. Abst. Surg.*, 83:313, October.

Markson, C. A. (1946). The Concurrent Use of Liver and Thiouracil, *Canad. Med. Assn. J.*, 55:22, July.

Cavanaugh, H. N., De Courey, C. B. (1946). Pharmacology and Therapeutic Aspects of Goiter, Thiourea and Thiouracil, *Ohio State Med. J.*, 42:1154, November.

R. W. CUMLEY, PH. D.

WAR ADVANCES ANESTHESIA

ONE of the fields of medical endeavor most advanced by the war was that of anesthesiology. For one thing, the professional status of the hospital anesthetist was greatly improved. He was a key man in most military installations, and his special virtues were more appreciated than they had been in civilian institutions. Further, an intensive training program increased by 50 per cent the number of skilled anesthetists. Various anesthetic agents were reappraised after studying on a large scale. Since the inflammable gases, ethylene and cyclopropane, were prohibited in Army hospitals, the anesthetist had to revive the use of nitrous oxide. In many, the results from this gas were a pleasant surprise, because in some respects it was found superior to cyclopropane. Nitrous oxide is non-explosive and produces no cardiac disturbances; induction and recovery are more rapid and pleasant. Pentothal sodium was found to have its greatest field of usefulness in operative procedures that do not consume more than 30 minutes, in which good relaxation is not essential, and when the patient is in good condition. Early in the war, as a result of misinformation as to the limitations of pentothal sodium, the mortality rate from its use was 1 in 450. But as the result of restrictions and better understanding of this agent, the mortality from pentothal dropped to 1 in 5,500 in spite of its increased use in combat areas. Procaine was confirmed as the safest all-round local anesthetic; and in doses up to 150 mg. was recommended as the spinal anesthetic agent of choice. Inhalation anesthesia with ether, or nitrous oxide-ether, was found to be the best anesthesia for patients in shock.

Suggested Reading:

McCarthy, K. C. (1946). War Advances Anesthesia, *Ohio St. Med. J.*, 42:1150, November.

Progress in Postgraduate Medicine



Doctors at the sickbed. Engraving by Chodowiecki 1781.



Postgraduate work under difficulties. Physicians in early American Colonies had a hard time studying the human body. Religious and other prejudices prevented them from obtaining study material. Drawing shows a group of medics who had to resort to body snatching, surprised by the police.



Surgical amphitheatre in the Massachusetts General Hospital during the second half of the 19th century.



In the Hospital, Painting 1889 by L. Jimenez.

The Bettmann Archive

Men of Medicine

Great Diagnostician

IT SEEMS quite in the natural order of things that he who was one of the most famous of diagnosticians should in the last of his cases "muff the diagnosis." And it seems quite proper too, as if to fulfill the demands of the dramatic dénouement, that the last of his cases should have involved none other than his own ailing and enfeebled person.

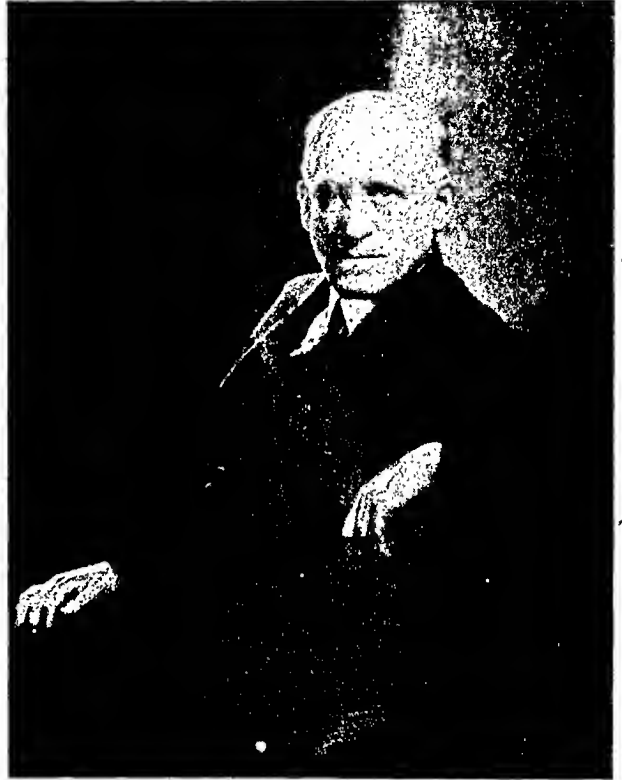
He diagnosed his case as an acute surgical belly, and so dominant was his authority that those who were called in to examine him would not gainsay him. Only the surgeon demurred, insisting that the clinical picture was not clear. Yet even he was prevailed upon to operate, though not until he had it set down in black and white that he did so under protest.

The belly was not acute. Such pathology as was to be seen was chargeable to the ravages of time.

The great diagnostician had muffed the diagnosis and he never recovered. On June 28, 1946, Emanuel Libman breathed his last breath on earth.

But the diagnosis was of little matter, for in any case death was not far removed. His thread of life had worn thin, and he himself knew it well. He spoke so long and so often of his oncoming exit that, impatient with the theme, I chided him in Milton's words:

"What need a man forestall his date of grief,
And run to meet what he would most avoid."



Emanuel Libman

Yet when the end did herald its proximity, he misread the signs. "This is not death that spears my side—it is some local hurt. A small incision; a quick extirpation; and in a jiffy, I'll be myself again." God rest his soul!

Emanuel Libman *was* an extraordinary soul. He was not cast in the common mold, and there is no measuring of him by the standards of everyday men. By those standards he is at once both too little and too great, that is, incomprehensible. But incomprehensible, he was not. It merely takes an uncommon slant to see him in his true perspective.

He was a friend to youth and to man in far the best sense of the term. Many, were they willing and able, could attest to his generosity, freely shown in every way, in aid, encouragement, and good counsel, given without thought of return or counter gain. Many among the elders were by his distinctive efforts saved from the misery and death that menaced them when the fury of the Hitlerite hordes engulfed Europe. He had a profound regard for character and for sound achievement. He hated humbug and pretense. Such he could transfix with a piercing comment. Of one among his contemporaries he said, "He speaks a false face English." Of a young psychiatrist he observed, "He has a large vacuole in his soul." He was eminently correct in both instances. But most remarkable was that though you were aware of the faults of both men, yet his phrases literally opened your eyes to precisely what was the fault.

He was a good hater, but he hated few men. He praised and admired more amply. He was full of fondness and admiration for Osler, but had a still higher regard for William Welch. Will Mayo was one of his heroes; so was Ehrlich, and he was fond of telling and retelling the story of how Ehrlich on his visit to America sought him out in his laboratory, even though some of the elder statesmen attempted to steer the Geheimrat along other paths.

He knew the elect in all walks of life both here and abroad. Some were his patients—Einstein, Boris Sokoloff, Sarah Bernhardt; others were his admirers, or his colleagues. The west wall of his office was covered with the autographed portraits of "his friends"—the Immortals of Medicine were all there—Horder, Noguchi, Osler, Welch, Cappel, Lewis. He was both modest and proud of this galaxy and passing by, would touch your sleeve and recount in his quick staccato voice some nugget of an adventure. And as he spoke, his eyes would twinkle and a thin smile would play about his thin lips. You were then made particularly aware of his extraordinary agility, of the nimbleness, speed, and dexterity of all his being. He seemed geared in a higher ratio, and all men were lumbering and cumbrous in his presence.

Neither his thoughts nor his speech were paced to a normal gait, but seemed rather to dart hither-

and yon in unpredictable directions. The effect was somewhat bewildering and he studiously cultivated the effect. He played with relish the role of the *wunder rabbi*. In Lindy's restaurant he was greeted effusively by a man whose father he had treated. Libman pretended he did not recognize him. But on being told the man's name, he recited forthwith the full history of the case, with some details of local color besides. The effect was magical. He had a prodigious memory. But he loved the theatrical effect. There was a touch of the Oriental about him and he preferred the Arabesque to the Gothic. This was reflected as well in his neckties as in the play of his mind. He was never devious in the manner of the timid and the malevolent, but he moved in arcs and spirals by a native preference. Add the nimbleness of his wit to the unorthodoxy of his orbits and you will see why he puzzled and bewildered so many of his contemporaries.

He had keen esthetic sensibilities, and was particularly responsive to music and color. He was also a cultivated gourmet. To dine with him was to experience a double adventure. An excellent repast was always assured, and with it a display of rare artistry in the blending of foods and drinks. Yet with all this he catered to his guests' tastes and was both knowing and mindful of their preferences. He was ever a gracious host, and always without ostentation. Yet he exacted his tribute. He rather talked than listened; rather led than followed the conversation. But who that had the privilege of his hospitality could begrudge him the tribute? He was a great raconteur; a great story teller. Some of the best of his tales were of the days when he practiced on the East Side, before he became a "so much."

When he was sixty, he was honored with a *Festschrift* and at seventy his many friends gave a dinner in his honor, filling the vast hall of the Waldorf. When he was dead, among the mourners that filled the Free Synagogue were men and women from every walk of life, Jew and Gentile, the wealthy and the poor, the famous and the unknown. They were there bound by the wish to pay tribute to a good man and a great physician.

Consultation Service

VAGUE ABDOMINAL PAIN AND LEUKOCYTOSIS

QUESTION: A male 40 years of age consulted me because of vague, generalized abdominal pain which developed insidiously and radiated directly through to the midlumbar vertebrae. Pain was aching, intermittent, lasting for an hour or two on the average once a day for one month, and nothing he could do would relieve it. There were no known precipitating factors and no relation to meals. There was no fever and no history of alcoholism. Physical examination was completely negative. Laboratory study showed normal 80 hemoglobin and 4,300,000 erythrocyte count, but there were 18,000 white blood cells with 80 per cent polymorphonuclears and no immaturity. Sedimentation rate (Westergren) was 8 mm. x-rays of the chest, blood pressure and pulse were normal. ECG, stomach, colon, gallbladder x-rays were negative. The roentgenologist said there was diverticulosis and some hypertrophic lipping of the lumbar vertebrae, particularly L3 and 4. Is the osteoarthritis sufficient cause of the symptoms? I can't explain the leukocytosis.

M. D.—Kansas

ANSWER: Osteoarthritis is not uncommon in the spine of patients this age or older. Granted he is slightly young for the more extensive type, people younger than he may be afflicted. The pain as described is not characteristic of osteoarthritis which is usually located primarily in the back, secondarily in other locations, but this is not a hard and fast rule. People with pain due to osteoarthritis find, as a rule, that work and physical labor aggravate the symptoms, and that the pain tends to be worse after retiring and not affected by limbering up. The pain and stiffness of rheumatoid arthritis on the other hand is worse upon rising in the morning or after sitting in one position for a long time, and is eased by exercise or moving about. Of the two

main types of arthritis, osteoarthritis and rheumatoid, the findings are consistent only with the former. Rheumatoid spondylitis is usually found in younger men and commonly shows X-ray changes in the sacroiliac joints. The sedimentation rate speaks for quiescent or absent infection, but the definite leukocytosis is as indicated and unexplained.

The lumbar spine x-rays (a-p and lateral) of many older people without back pain reveal hypertrophic osteoarthritis which is called an incidental finding, while the same roentgenologic picture in the presence of pain is generally considered evidence of cause. The doctor is thereby relieved to find a place to hang his diagnostic hat. A famous doctor, once called upon to explain the mechanism of the pain of osteoarthritis, said that at a meeting some years ago he had been called upon to explain this very phenomena after having a few cocktails before the meeting. "I gave them a wonderfully complete explanation," he said, "but now I have forgotten it."

It would seem that osteoarthritis must be the last hatrack after we have eliminated the others; first because the clinical story, incomplete as it is, is not characteristic; and secondly, another diagnostic problem, perhaps more amenable to therapy, may be overlooked. The mild anemia is of little help.

The diagnosis of diverticulosis in adults is common and of itself of no clinical significance. The roentgenologist can usually ascertain the presence of diverticulitis, but not with 100 per cent accuracy. The story again does not suggest diverticulitis because while acute diverticulitis resembles "left-sided appendicitis," chronic diverticulitis may give a thick-walled, palpable abscess in the left side of the pelvis. Diverticulitis, common in the age group 40-60, usually gives a long, intermittent history; tenderness and pyrexia are common, and on x-ray, the bowel typically shows strictures. There is usu-

ally leukocytosis. Every case of diverticulitis has an inception. It is conceivable that this is the beginning of the disease, but not likely. Sigmoidoscopy would help resolve the problem.

X-ray examination of the small bowel is usually unsatisfactory, but lesions may occasionally be found. The pain in obstructive lesions is apt to be more colicky in type and associated with vomiting. Regional ileitis must be considered.

In chronic relapsing pancreatitis, the pain is usually more severe with a long history and associated with a steatorrhea. If the pain persists, an excretory urogram should be made. Perhaps it would give the answer immediately. Repeated urinalysis should be made at once if not already done. Therefore we are left to explain a leukocytosis of considerable magnitude, in the absence of evident infection and a normal sedimentation rate. The causes of leukocytosis are too manifold to mention, but if we can be certain that infection is ruled out (which is not certain from the information given but which we may assume for the sake of discussion), then the one disease which must be considered is leukemia of the aleukemic type. A sternal biopsy may reveal abnormal cells. If this is in reality the cause of the leukocytosis, possible retroperitoneal infiltration may be the cause of the pain. One would expect either a palpable spleen or lymph nodes or both. I presume no palpable nodes were found. Careful, repeated white blood cell counts and differential diagnosis may reveal immaturity at one time or another. The white count must be followed until normal. A neutrophilic leukocytosis follows sudden loss of blood. This is present frequently in persons suffering from malignant disease, especially of the gastrointestinal tract. It results from certain drugs and poisons including carbon monoxide, lead, turpentine, and castor oil. There is no evident purulent infection in this case which causes high counts. One must consider exposure to poisons or drugs as an important diagnostic point, especially lead. Without basophilic stippling, blue line on the gums, peripheral neuritis, the test for lead in the urine would probably rule this out. The absence of anemia and rapid sedimentation rate are against multiple myeloma.

And finally, one must remember that while any doctor can diagnose about 85 per cent of cases, no one can diagnose many of the remaining 15 per cent. True, a few can be tracked down, but there is always a group in which no diagnosis can be made with certainty. Many of these develop a full-blown disease later; many recover and always remain obscure; the others go on with the symptoms either unsatisfied because their doctor has told them he does not know what the problem is, or satisfied with "colitis," "chronic appendicitis," "arthritis," "neuritis," and the others. In this case it is barely conceivable that all of the symptoms are due to osteoarthritis but why the leukocytosis? If further study fails to throw any more light on the problem, it is best to reserve judgment and study the case again in another month or two. A case of periarteritis nodosa, lupus erythematosus, dermatomyositis, may be lurking. It is my opinion that we cannot arrive at a diagnosis without more data or the lapse of more time. I would favor leukemia, carcinoma of the bowel, small intestine and periarteritis nodosa as the most likely in the order named.

Editor's Note: At an exploratory laparotomy subsequently performed, carcinoma of the cecum with metastases to the retroperitoneal lymph nodes was found.

MASSIVE VOMITING OF BLOOD

QUESTION: A patient 60 years of age first vomited about one quart of fresh red blood three months ago. There was no pain and, aside from the weakness which ensued, no subsequent symptoms until a second hematemesis one month later. This was followed by a third and a fourth, each of large quantity. X-ray studies elsewhere failed to reveal any lesion in the upper gastrointestinal tract. The patient sought a different medical consultant who ordered another barium x-ray which was interpreted as showing extensive carcinoma of the entire stomach. On this basis he was told he had cancer and that surgery was not advised. There was no rectal shelf, but a smooth large liver and spleen were palpable, and there was slight dependent edema. He had had an hemorrhoidectomy

four months ago. He is now under my care, and despite the loss of 25 pounds of weight, I am inclined to favor exploration. Under the circumstances, would surgery be justified?

M. D.—Missouri

ANSWER: This extremely interesting case presents several points concerning which there is room for justifiable difference of opinion, and in which there may have been committed serious errors. In the first place the patient was told he had cancer—I presume the word was used—when in fact this was not really known. The x-ray diagnosis of gastric lesions in good hands is remarkably high, but far from infallible. Thus, it seems that the *error of implicit belief in the x-ray* was committed, this, even if he actually has cancer, for without tissue examination or evidence of metastasis there is no proof. Massive hemorrhage of this type, although occurring in cancer of the stomach, is rare. Second, the *error of hidden historical facts* may have been committed, for although hemorrhoidectomy is a common operation, and though dependent edema is not uncommon in a man 60 years old, particularly after loss of blood proteins, nevertheless, these two, together with this history of emesis of bright red blood (not coffee ground) coupled with a palpable smooth liver and spleen suggest the possibility of bleeding esophageal varices on the basis of portal obstruction due to cirrhosis. Finally, there may have been committed the *error of failing to come to grips* with the problem. To this end a third gastric X-ray, or gastroscopy might solve the problem, or, as you suggest, surgery. If this is cancer, and if the entire stomach or a considerable portion thereof is involved, and there has been hesitation for several months, it seems unlikely that successful resection could be undertaken.

There are probably distant metastases. Nevertheless, the remote possibility of no metastases does exist, and if a repeated chest x-ray is negative, the liver still smooth, and no palpable nodes or rectal shelf, surgery might be undertaken. If the case is one of Banti's disease, the spleen should be removed.

The question always comes up as to whether the patient should be told he has cancer, and although there are many opinions on the subject, it is the

writer's strong feeling that a patient should be told he has a "tumor," his relatives told that he has cancer. If the patient asks point blank, "Is this cancer?" the doctor is obligated to reply in the affirmative, if it is his absolute opinion that such is the case. In the absence of proof, he must say that such is his opinion. Can the patient be urged to submit to surgery? The answer is probably no. He can only be informed of the risks and the possible advantage.

BLEACHING OF HAIR

QUESTION: A patient of mine is in the habit of bleaching her hair periodically with a mixture of hydrogen peroxide (20 vol) and ammonia (about 2 parts to 1 part). She has been informed by a hairdresser that this will eventually destroy the hair roots. Is this true? If not, is there any danger?

M. D.—Louisiana

ANSWER: According to Savill, hair bleach, as well as hair dye, discourages the growth of hair. Repeated bleaching renders the hair fragile, producing crinkly hair which frequently breaks in many places when combed. There is no evidence, however, that there is permanent alteration of the hair follicle as the result of repeated bleaching with the mixture of hydrogen peroxide and ammonia.

REMOVING TATTOO MARKS

QUESTION: What is the best way to remove tattoo marks?

M. D.—California

ANSWER: There are three approaches to the removal of tattoo marks: surgical, electrolytic, and chemical. Surgical excision with or without a graft is most effective, depending, of course, on the size and location of the tattoo. Numerous other measures have been recommended, most of which result in scarring. The tattooed area can be re-tattooed with a 50 per cent solution of tannic acid, followed by the application of silver nitrate cream. The use of direct irritants or the removal of the pigmented particles with an eye curette has also been recommended. Direct irritation of the skin with 30 parts

of zinc chloride and 40 parts of water is of dubious value.

MULTIPLE WARTS

QUESTION: *A schoolboy, apparently in perfect health, has a mass of warts on his hands and knees and they are now appearing on his lips and face. This is a distressing condition and I shall be grateful for advice. Cauterizing the warts individually would be an impossible task.*

M. D.—Idaho

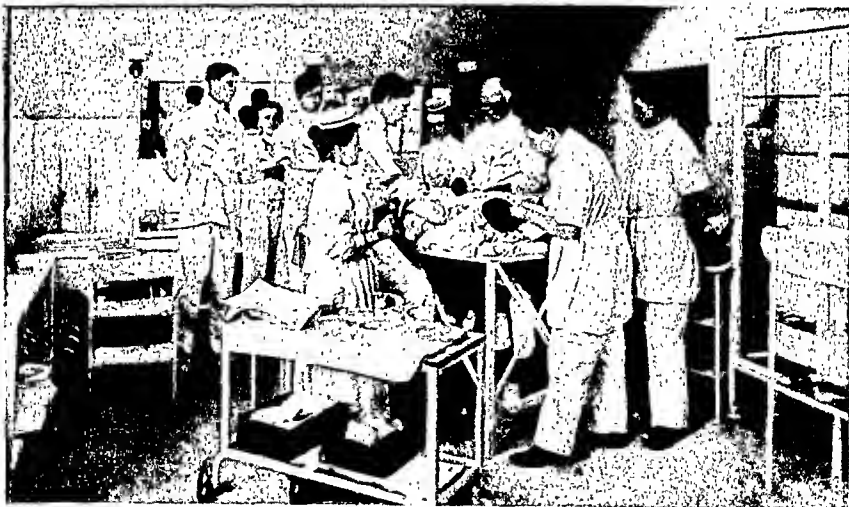
ANSWER: Superficial roentgen therapy is frequently of benefit for the removal of multiple warts. If this therapy is not effective, carbon dioxide snow as direct irritant to the warts is recommended. Mercury or arsenic by mouth is of definite value. A course of bismuth subsalicylate, 1 cc. intramuscularly once a week for twelve injections, is effective in about half of the patients.

REMOVAL OF SUPERFLUOUS HAIR

QUESTION: *I remember seeing a preparation of barium recommended for safe and reliable method of removal of superfluous hair. Would you please say which barium salt is suitable for the purpose and give particulars of its application?*

M. D.—South Dakota

ANSWER: Barium sulfide is a depilatory for removing the hair without affecting the papilla. There is a regrowth of hair, however, in approximately two to four weeks. The prescription for the use of this is: Rx. Barium sulfide 8; pulverized zinc oxide and pulverized amyl, ea. 12. This should be mixed with warm water just before it is applied to the face as a paste. A spatula should be used to spread this mixture to the hairy surface where it remains for approximately five to ten minutes. It is then scraped off and the face should be washed with warm water and cold cream applied.



The Fitzsimons Archive

Historical Epochs In Medicine: Professor Charles McBurney (1845-1931), famous for his discovery of the "McBurney point" as a sign for operative intervention in appendicitis, operating in Roosevelt Hospital, New York.

What Other Editors Think

Editorial Evaluations of Current Contributions to Medical Progress

MASKING OF SYPHILIS BY PENICILLIN

MUCH emphasis has been placed on the possibility of penicillin therapy in gonorrhea altering or masking the customary development and the signs of a syphilitic infection acquired with or prior to the gonococcal infection. That this is not without reason is supported by the accumulating experiences of many who engage in the treatment of large numbers of patients suffering from venereal diseases.

In the patient treated for gonorrhea with penicillin, a syphilitic infection acquired either before, at the time of the gonorrheal infection, or later, may or may not be appreciably delayed in development, and then pursue a usual course with the formation of a chancre; or without the appearance of a chancre may be evidenced by the presence of generalized lymphadenopathy, or clinical manifestations of secondary syphilis or by a positive blood test. It follows then that any patient treated for gonorrhea with penicillin must be strongly warned to submit himself, at the least, for monthly blood tests for four months after receiving the drug.

Treatment of early syphilis with penicillin is accompanied by a Herxheimer reaction in about 90 per cent of all cases, while treatment of gonorrhea is rarely accompanied by fever. For example, in one series of 2,000 penicillin treated cases of gonorrhea, which did not present evidence of syphilis, only three patients were observed to have a febrile reaction which could not be explained on the basis of a toxic reaction to the penicillin or to the coexistence of syphilis. All of this strongly suggests that the occurrence of fever with penicillin treatment of gonorrhea indicates the coexistence of syphilis.

The foregoing discussion supports the admon-

ition that penicillin treated patients be kept under strict clinical and serological supervision during the suggested four months observation period.

Macnish—The Urologic and Cutaneous Review, Vol. 50, P. 580

LEUKOCYTIC COUNT IN INFECTIOUS HEPATITIS

HAVENS and Marck have had the unique opportunity of observing a series of patients who had experimentally induced infectious hepatitis. These subjects were healthy male human volunteers whose age varied between 19 to 29 years. In addition to their observation on the course of the disease, the symptoms that the patients presented, and the other findings more or less characteristic in infectious hepatitis including jaundice, they made serial observations on the leukocytic response during the incubation period of the disease and its course. It is the response of the white cells to the virus that we wish to comment upon because the leukocytic count is of value in the diagnosis of this interesting disease which has become so frequent during the war period when large groups of young people were collected together.

Twenty-six patients are reported upon in detail. It is to be noted that the leukocytic response begins in the first twenty-four to forty-eight hours of fever and it is associated with the febrile pre-icteric phase of the disease. There develops early a leukopenia, a leukopenia which involves both the neutrophils and the lymphocytes. The charts of these observers show that there is a sharp drop in the total count which may fall as low as 2,000.

The average count is approximately 4,000. With

the development of jaundice the count rises gradually to a level between 6,000 and 7,000. The return to normal leukocytic relationship occurs by the end of the second week after the fever has appeared. There are exceptions of course and counts as high as 11,000 may be observed but, as noted before, the average count at time of the fever when the diagnosis is in abeyance because jaundice has not yet appeared, is low.

It should be noted further that there often appears a relative lymphocytosis with numerous atypical lymphocytes. The monocytes are sharply depressed while there is fever. The abnormal lymphocytes producing a relative lymphocytosis are often of the large type so that large lymphocytes may form in as many as 40 to 70 per cent of the total number. A few of these large cells are atypical in appearance so that their discovery may be of diagnostic importance.

Infectious hepatitis, now known definitely to be a virus disease, is sometimes difficult to recognize before the appearance of jaundice. A series of careful blood counts may be of some help in determining the febrile disease which a patient may have and of which the cause is unknown, prior to jaundice.

*New Orleans Medical and
Surgical Journal, Vol. 99, P. 182*

CHOLESTEROL IN PROTECTION OF ARTERIAL LESIONS

OFTEN in research work it is wise to perform at the outset what appears to be a crazy experiment. For instance, years ago, chemists who were trying to find an organic compound in liver which would influence blood formation decided that they would go to the limit in the other direction and try the effect of some liver, ashed. To their astonishment they found that the ash did affect the formation of blood.

At the last meeting of the American Society for Experimental Pathology (Federation Proceedings, Vol. 5, February, 1946, pp. 223-224), Russell L. Holman of the Department of Pathology, School of Medicine, University of North Carolina, Chapel Hill, reported that in dogs with induced renal insufficiency he had been able, by changing the

diet, to produce arterial lesions affecting primarily the inner layers of large arteries. The renal insufficiency was produced by toxins, such as uranium nitrate or mercuric chloride, or by bilateral nephrectomy. Some degree of renal damage was essential if the arterial lesions were to be produced. The injurious factor in the diet was found in concentrated form in commercial cod liver oil: It is heat stable, not readily oxidized, and is neither vitamin A, nor vitamin D.

To Holman's astonishment he found that the giving of cholesterol would protect against the formation of the arterial lesions. If this should be confirmed by further studies, the fact may alter some present theories about the dietetic treatment of persons with atherosclerosis.

W. C. A.—Gastroenterology, Vol. 7, P. 575

VITAMINS AND VITALITY

LITTLE publicity has been given to the saga of Balto the dog-mascot to a dispensary on the Alaska highway. Balto, it seems, chewed his way into a supply carton and swallowed several hundred vitamin tablets. What happened to Balto? Nothing. He did not zoom over the tundra or chase away a pack of wolves. Nor did he burst from any internal explosion. To the dismay of the pharmaceutical industry, Balto remained quite the same after his vitamin orgy as before. This unintended experiment in the efficacy of vitamins was matched on a smaller and more realistic scale, earlier this year when Branshy and his colleagues (*British Medical Journal*, 1:193, February, 1946) published the result of a study of supplementary vitamin feedings to children. One group of children received a capsule containing an inert placebo. The other group received a capsule loaded with vitamin A, riboflavin, ascorbic acid, vitamin D and nicotinamide. The project was faithfully followed for a full year. The supplementary vitamin, according to these authors, "had no consistent effect on growth, strength, endurance, fatigue, clinical conditions, or absenteeism from school."

This does not mean that a clinical syndrome would not have resulted had the diet been deficient in vitamins. It does suggest, however, that

the available diets, even in contemporary Britain, have all the vitamins that the organism can utilize.

*Journal Medical Society of
New Jersey, Vol. 43, P. 487*

CRITERIA OF IRREVERSIBLE SHOCK

IN STUDIES of shock in dogs, Wiggers and Ingraham, of the University of Chicago, have developed a technic for withdrawal of blood to maintain hypotension for a period of ninety minutes. Clotting of the withdrawn blood is prevented, and subsequently all of it is returned to the veins of the animal. The animal may thus conveniently be studied in the shock state.

Acidosis usually develops as the blood pressure falls, so continuous intravenous injections of alkalinizing agents, either sodium lactate or sodium bicarbonate, were administered. It was soon observed that lactate did not successfully combat the acidosis, but bicarbonate was much more effective.

In the dogs which died in shock, acidosis prevailed. In those which recovered, bicarbonate had been administered through the shock period, so that acidosis did not develop. Development of acidosis with low carbon dioxide capacity was considered an indication of irreversible shock. Uncorrected acidosis may contribute to or hasten development of severe and irreversible shock. Administration of bicarbonate considerably reduced the mortality rate.

Criteria of irreversible shock are: spontaneous and the persistent decline of arterial blood pressure. A dog with persistent declining tendency of the blood pressure in shock rarely recovers. The passage of bloody feces after withdrawn blood has been restored was also an indication of irreversible shock. And a markedly fast post-reinfusion heart rate was an indication. A rise of heart rate of 150 or more per minute within five or ten minutes after reinfusion was ominous. Satisfactory post-reinfusion arterial blood pressure did not indicate that the animal would recover.

They attempted to produce irreversible shock in dogs by giving them large doses of histamine. The blood pressures could be reduced to 35 to 50 mm. of mercury and kept there for three hours and longer, during which time severe acidosis existed. But only a third of the animals developed

irreversible shock. It was considered that the vasoconstriction which follows hemorrhage is important in development of shock. Vasoconstriction does not occur in histamine hypotension.

Southern Medical Journal, Vol. 30, P. 671

RIGHT HEART CATHETERIZATION

INASMUCH as advances in medical research are so frequently associated with the introduction of new techniques of investigation, the increasing use of right heart catheterization in cardiovascular studies is worthy of note.

In 1941 Cournand and Ranges described the technique in detail and since that time numbers of workers in America and overseas have published their experimental experiences with this means of investigation. Thus, in a Symposium on Cardiac Output of the American Physiological Society a year ago, Cournand was able to state that the method "has proved its safety in well over 1,200 cases, not only in ours but in the hands of a number of other investigators in England and in this country."

It is possible by his method to obtain mixed venous blood from the heart in order to have data necessary for the determination of cardiac output by the direct Fick principle. The catheter has also been passed through the right atrium and on into liver radicles or into the renal vein to obtain blood samples from these regions.

Problems studied include the effects of blood loss, posthemorrhagic fainting, shock, right heart failure, chronic anemia and digitalis upon cardiac output and right auricular pressure.

In a recent report the practical advantages of heart catheterization in the differential diagnosis of congenital heart disease are demonstrated. These workers placed the tip of the catheter in a variety of locations within the heart and pulmonary tree and by a study of the oxygen content of samples taken at different sites were able to chart the route taken by the blood in an abnormal heart more accurately than has heretofore been possible. The knowledge so gained is obviously of great importance as regards whether or not surgery is indicated.

*Canadian Medical Association
Journal, Vol. 55, P. 392*

BENIGN STRICTURES OF THE BILE DUCT

STRICTURE of the common or hepatic bile duct most often follows clamping, ligation or excision of the duct during cholecystectomy. The common duct will not be injured if it is clearly seen. The first necessity is adequate exposure with accurate definition of the junction of the hepatic, cystic, and common ducts before anything is clamped or cut. If this rule is followed, most of the hazards are eliminated. Injury occurs with inadequate exposure, inflammation or impaction of stones that shorten the cystic duct, strong traction on the gall bladder that tents up the common duct, anatomic abnormalities that confuse the relations, and blind efforts to control bleeding.

If the surgeon discovers a damaged or severed common bile duct, it should be repaired immediately for it is never easier to do later. The two ends of a divided duct should be united by end-to-end anastomosis. If a T-tube is used, the vertical limb should not come out through the suture line but rather above or below it. A duct that has been crushed by a clamp should be allowed to heal over a tube. If it is badly macerated, the devitalized tissue may be excised and an end-to-end anastomosis done.

The end-result of an unrepaired common duct injury is biliary fistula or stricture with devastating sequelae. Small strictures are not so serious for they may often be successfully treated by plastic repair or by excision and end-to-end anastomosis. The real problem concerns those who have extensive stricture or loss of the duct, often complicated by repeated, fruitless attempts at repair and usually associated with anemia, hypoproteinemia, infection, and liver damage. These may often tax the fortitude, patience and ingenuity of those who seek to repair them. No one method is applicable to all cases. In general, two methods of attack have been used; either anastomosis of the duct to the intestine or reconstruction of the duct. Of the former, anastomosis of the duct to the duodenum has been used most frequently but only 23 per cent have a successful end-result (Eliöt.) The Roux Y type of choledochojejunostomy, popularized by Whipple, is a more physiological intestinal anastomosis since

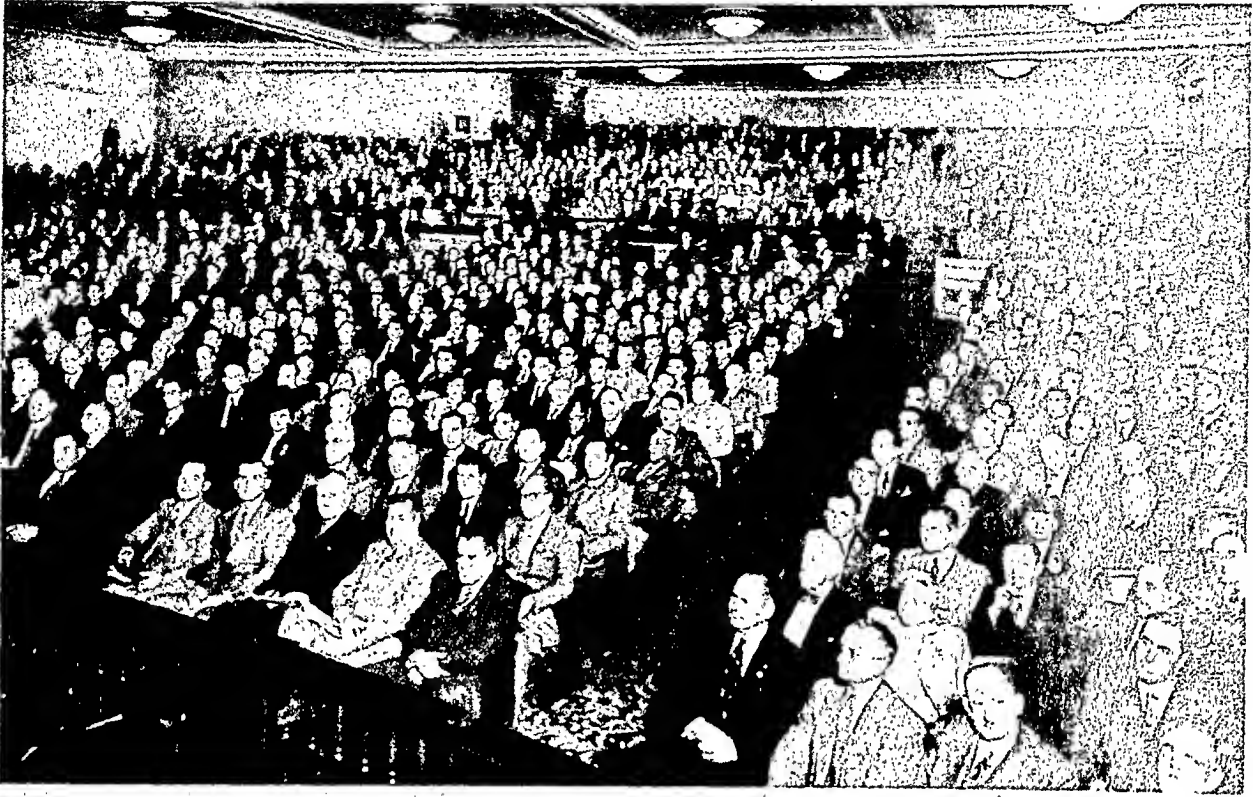
the antiperistaltic loop of jejunum prevents reflux of intestinal contents into the biliary tract.

It appears desirable, whenever possible, to restore the normal anatomical arrangement of the part for few surgical procedures improve on nature. For this reason, even with extensive loss or stricture, efforts should be made to reunite whatever remains of the duct. This union may be possible only with tension on the suture line which permits reformation of the stricture. To prevent stricture the duct should heal over a tube which holds it open during repair. Dissatisfaction with the tissue irritation and fibrosis caused by rubber led to the use of vitallium for this purpose. Vitallium was selected because of its lack of tissue reaction, its smooth surface which did not attract concretions and its high tensile strength which permitted a thin wall with maximum lumen. Tantalum also has these characteristics and is more malleable but it cannot be welded, so no anchoring flange can be attached to it. Plastics were discarded because most of them are tissue irritants. Vitallium tubes have the disadvantage of being so hard that they cannot be altered, at the time of operation, to meet the needs of every situation nor is it possible for them to be removed except by an operative procedure.

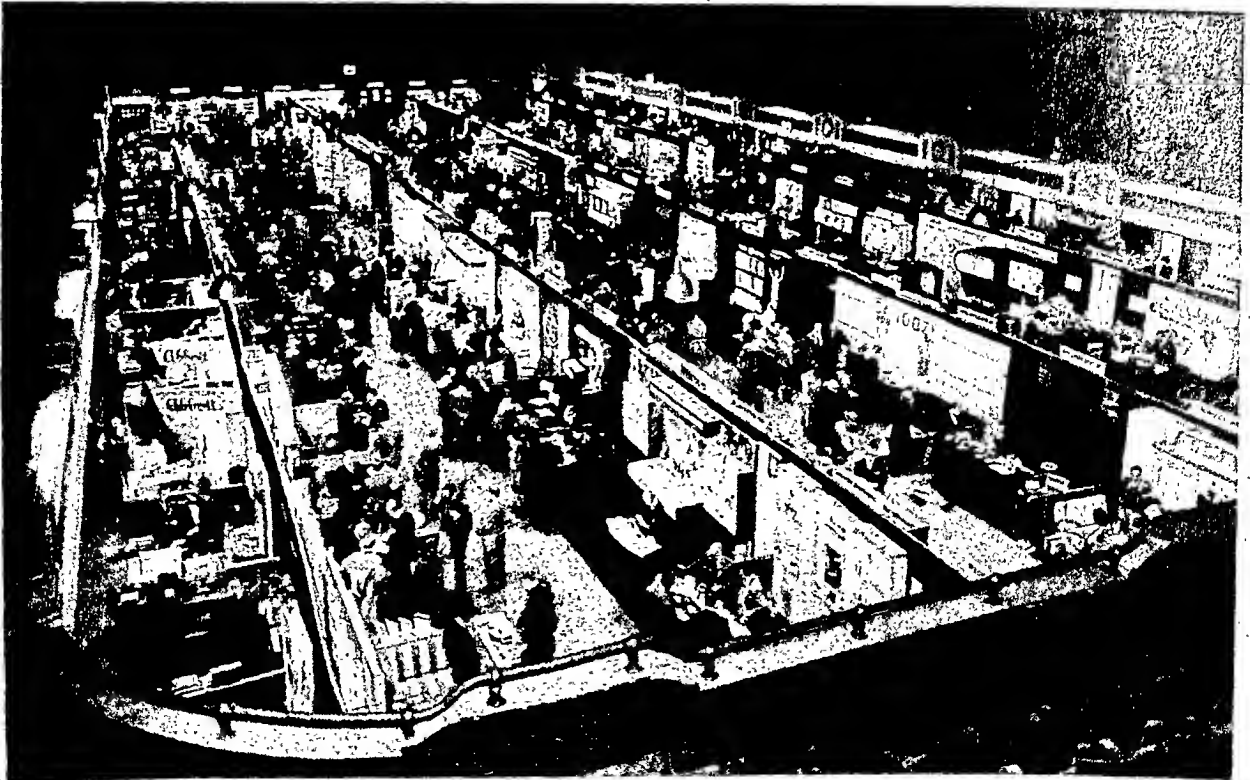
Recently, 226 cases of the use of vitallium tubes were collected from a group of surgeons and the results studied. The outcome was satisfactory in 80 per cent of the cases when the tube was used for the reconstruction of the duct. Plugging of the tube occurred in 11 per cent and was the commonest cause of failure. Plugging may be diminished by using bile salts postoperatively but metabolic changes and infection make it difficult to eliminate occlusion of the tube completely. Anastomosis of the duct to the duodenum over a vitallium tube gave 58 per cent satisfactory results. The tube passed into the intestine in 38 per cent of the cases. This sequela is to be expected for no amount of anchoring will prevent the loosening of the tube. The results of Whipple's Roux Y anastomosis are still better for it is a more physiological operation.

Herman Pearce—Surgery, Gynecology and Obstetrics, Vol. 83, P. 549.

The 1946 Meeting



1946 Program appreciated by receptive and indefatigable audience.



The large Technical Exhibit was replete with new drugs, new instruments and new appliances.

Interstate Postgraduate Medical Association Notes

CLEVELAND ASSEMBLY

October 14 to 18 inclusive, 1946

THE thirty-first year of our postgraduate medical teaching enterprise found our Assembly adequately housed in the splendid Cleveland Public Auditorium. Earnest doctors came from all of the states in the Union as well as many from abroad. Pleasing indeed was the greatly increased attendance of Canadian physicians, who were notably absent from our 1944 meeting due to the war and to the Canadian foreign exchange restrictions. No less gratifying was the attendance from California—proportionately larger from the standpoint of registered physicians per state than any excepting Ohio, where the meeting was held.

The large Technical Exhibit was especially noteworthy, replete with new drugs, new appliances, and new instruments, many displayed for the first time since our last Assembly in 1944, when shortly thereafter, the war ban enjoined the holding of large gatherings. The demonstrators did their full share in answering endless questions, and they contributed vastly to the general educational offerings at the meeting.

One hundred seventy-eight leading drug, instrument, and appliance manufacturers occupied two hundred thirty booths, filling to overflowing the excellent Exhibit Hall, brilliantly lighted with the special illumination installed for our needs.

As always, each teaching session started "on the dot" as scheduled, and the varied program with up-to-date instruction given by nationally recognized leaders in their respective fields was appreciated by a receptive and indefatigable audience, as evidenced by their reactions, and later reiterated by a flood of commendatory letters.

One of the outstanding events of the meeting was the decision by the Board of Trustees to discontinue the issuance of the Proceedings in a single volume. It was determined that henceforth the clinics and the addresses given at the annual meetings would be published exclusively in the new official magazine of the Interstate Postgraduate Medical Association, *Postgraduate Medicine*.

On the third evening of the Assembly, instead of the usual night lecture courses, the annual

dinner was held in the largest dining room in Cleveland. Nearly a thousand were seated, filling the room to capacity, and others who were unable to purchase dinner tickets came later to hear the remarkably interesting addresses.

The retiring president, Dr. Donald C. Balfour, Director of the Mayo Foundation for Medical Education and Research, Rochester, Minnesota, gave a beautifully illustrated lecture entitled, "An Outline of Medical History." It was a delightful, comprehensive summary of the halting progress of medicine through the ages, and depicted the groping and the uncertainties—until about fifty years ago when, with explosive suddenness, and chiefly through the displacement of empiricism by the ascendancy of research, the scientific tempo began to race. The development of the specialty fields and the incredible advances made, resulting in ever better and more dependable methods of diagnosis and treatment, from the combined efforts of scientists and artisans in all lines, has placed America far in the lead, and occasions constant wonder at the startling new developments in medicine which lie ahead.

The address by Colonel Ashley W. Oughterson, Medical and Scientific Director of the American Cancer Society, Inc., New York City, was a gripping, illustrated discourse concerning his investigations at Hiroshima and Nagasaki, of the effects of the Atomic Bomb, notably on humans in Japan. The unbelievably intense effects of the heat, of the blast, and more especially of the wide lethal radiation of devastating long-lasting electronic elements, were revealed by numerous slides which portrayed with an unforgettable vividness the horrors of atomic energy when employed as a destructive agent.

The brief acceptance address of Dr. James E. Paullin, Professor of Clinical Medicine, Emory University School of Medicine, Atlanta, Georgia, who succeeded President Balfour at this meeting, was gracious and humorous. President Paullin paid tribute to the past accomplishments of the Interstate Postgraduate Medical Association, and indicated he would lend his hearty support to

ning of a quarter century of medical progress which probably has no counterpart in history.

"In addition to the Academy of Medicine welcoming you to Cleveland, Mr. Burke, the honorable mayor of the City of Cleveland, asked me to give you the official welcome of the City of Cleveland."

Dr. Crawford then introduced the retiring president, Dr. Balfour, professor of surgery at the Graduate School of Medicine, University of Minnesota, and Director of the Mayo Foundation for Medical Education and Research at Rochester, Minnesota. He spoke as follows:

"I feel it a great privilege and honor to be presiding here this evening. When you look back over the history of this organization, some 31 years, those of you who have been as loyal as most of you are to the organization will know what I mean when I say that I do not know of any organization which has kept the panorama of medicine so clearly before those who attend the sessions.

"To preside at this particular meeting is an unusual honor and privilege, because a great deal has accumulated since the last meeting in the way of knowledge, and the dissemination of that knowledge by the speakers who have been on this program has been something which I am sure you will all remember. For that reason, I should like at this moment to express to the Board of Trustees and to the local committee, of which Dr. Russell B. Crawford is chairman, and to Dr. Charles S. Higley, chairman of clinics, the very grateful thanks of you all for the magnificent program which they have put on for you."

JAMES E. PAULLIN, 1947 PRESIDENT

Dr. Paullin, president-elect of IPMA who was introduced by Dr. Balfour, said:

"It is with a great deal of humility that I enter upon the arduous duties of this office. For a poor, humble internist to follow such distinguished men as Frank Lahey, Fred Rankin and Donald Balfour, is an honor greatly appreciated by the humble ranks of your profession.

"I am very happy to head an organization such as this because it represents to me one of the greatest groups of physicians that we have assembled together—men and women who are associated in the general practice of medicine, people who take care of the sick. It is wonderful on occasions such

as this to have this group together and to have brought to them the greatest developments in the various specialties, because these men—you and I and a lot of others—go back home to put into practice the things that we have learned here.

"There is not any greater field in medicine than that of education. I have been vitally interested in that for 40-odd years, having been an instructor, a teacher, a professor in medicine at Emory University in Atlanta. There is not any greater contribution that a man can make to his profession than in education, for in education he not only imparts knowledge but he himself becomes a better practitioner of medicine because he learns. If at any time in the course of a doctor's career he ceases to learn or to become instructed, somebody ought to take him out and give him some of Crawford W. Long's ether anesthesia.

"It is a wonderful occasion to meet with friends whom we have known for years and to welcome back into these meetings men who have given their service to their country during these past few years. No one knows better than I of the sacrifices which these men have made. I have seen them in the Army, I have seen them in the Navy, I have seen them in the Atlantic, I have seen them in the Pacific, I have seen them in our own country. No one can ever write a tribute to the members of the medical profession who entered World War II and who accomplished such brilliant results, no one can ever write a eulogy which will be equal to their attainments. They have not received the recognition that they should have had. We know that, I know it, you know it; but they have the consciousness of having done a job, of having done it well.

"We are approaching a period in world history that is going to be quite romantic. I hope I shall be able to carry on the traditions of this Assembly along the lines which have been outlined before. I do hope that as a result of these meetings and the thoughts that you carry back home, the reports that you make of what has been said here to your county and local medical societies, the medical profession itself will be elevated constantly to that tradition which we all hold close, of becoming better doctors, taking better care of our patients, and rendering to them a service which is unexcelled."

The Doctor in Literature

It is true that the professions of theology and law have contributed more to literature than has medicine, but in spite of this we like to think Chisholm was wrong when he said, "So few are those who have entered literature through the gateway of medicine, that it seems almost as if Apollo had disinherited his son Esculapius." However, even a casual search reveals a wealth of material, and we find that physicians from the time of Hippocrates have contributed a considerable amount.

* * *

The Hippocratic Oath is one of the world's finest pieces of prose writing, besides being one of the greatest of moral concepts. Shortly after the time of Christ, St. Luke, the great Hebrew physician of the New Testament, wrote the gospel which bears his name. He wrote with such a clear and scholarly pen that he justly ranks as one of the better writers of the world.

As we look into the literature of the various modern countries for contributions from medical men, we find Francois Rabelais, the French humorist, and Clemenceau, the author and statesman. In Russia, A. R. Chekov published plays and short stories, and in Germany Schiller and Goethe are best known. British names are legion—*Religio Medici* is probably the best known work of the classical scholar Thomas Browne. An early seventeenth century contemporary of his was Abraham Cowley, who wrote the poem, *Pyramus and Thisbe* at the age of nine. Scanning the long list

we might pick out such outstanding men as Oliver Goldsmith. John Keats, Thomas Henry Huxley, William Osler, A. Conan Doyle, and Charles Scott Sherrington.

American physicians are entitled to their share of contributions to literature. Pennsylvania gave us Benjamin Rush and S. Weir Mitchell. An idea of Dr. Mitchell's virility of mind, at an advanced age, may be obtained



by recalling that he wrote *Westways*, a successful novel of buoyant youth, when he was eighty-four years old. Massachusetts' Oliver Wendell Holmes, who gave to medical science the first real conception of puerperal fever was, in literature, a master of two media—poetry and prose.

New York's Joseph Collins, professor of neurology in the New York Postgraduate Medical School, was well known as a literary critic. He made some studies of medical men in literature (*The Doctor Looks at Literature*) which are still admired.

In the history of American letters, few men have had a Boswell equal to Harvard's Hans Zinsser, whose deep learning and salty wit made a book of the story of typhus fever, *Rats, Lice and History*. The influence of his work and writing swell into tidal waves which sweep the shores of medical thought. Before he died he wrote his auto-

biography, *As I Remember Him*, a remarkable book which is, indeed, a legacy to this generation from a great doctor.

Harvey Cushing, eminent as a surgeon, won a Pulitzer Prize for his *Life of Sir William Osler*; he now has the spotlight turned on him. Charles C. Thomas recently published a biography of Dr. Cushing—the man who wanted above all things to be a good doctor—written by Dr. John Fulton, Yale physiologist. As Dr. Cushing's literary executor, Dr. Fulton began this biography soon after Cushing's death, and writes with simplicity and deep understanding. It is an absorbing story of the growth of medical science through half a century, and a glowing tribute to the importance of "pure" science.

Both Holmes and Cushing liked to quote on occasion from *The Diary of The Rev. John Ward*, middle seventeenth century vicar of Stratford-on-Avon: "There are several sorts of Physicians, said one; first, those that canne talk but doe nothing; secondly, some that canne doc but not talk; thirdly some that can both doc and talk; fourthly, those that canne neither doe nor talk—but these get most monie."

* * *

Books are legacies which mankind delivers as presents to the posterity of those yet unborn. These babies just being born are going to grow up to read a lot of books about medicine and, of course, some of these will be written by doctors. "We'd like to have a nickel," report the editors of *Cosmopolitan*, "for every manuscript we've seen in the last six months that has been con-



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cerned with such things as palsy, alcoholism, psychoneurosis, diet, or atomic fission. The favorite theme of most writers today is medicine and, in particular, psychiatry." We are told by those in the trade that most story-tellers, even non-fiction writers, have dropped war themes.



Some years ago an article in *The Saturday Review of Literature*, noting the popularity of books about Lincoln, doctors, and dogs, suggested that an all-time best seller would be a book entitled *Lincoln's Doctor's Dog*. Judging by today's trend, it seems that someone has a chance to go a step further and top this by writing an extraordinary volume to be called *A Psychiatric Study of Lincoln's Doctor's Dog*.

* * *

Thoughts expressed in words are imperishable. Some of the words, however, are ever so hard to pronounce. According to Charles D. Rice, the editors of Webster's New International Dictionary, think they have discovered what may be the longest word in the dictionary. The word is a medical term meaning a lung disease that miners are liable to contract. Today it appears in the New Words Section, dragging its tail through a whole line of type. In case you are serious about this and want to settle a bet, here it is—a jawbreaker: *pneumono-ultramicroscopic-silicovol-cano-koni-osis*.

POETRY: Browning said, "Unlock my heart with a sonnet-key." Either the weary, routine dullness or the very deep-felt excitement of medical duties give doctors a natural desire to write a sonnet or a ballad—to be lyrical and tuneful. With all the talk about relative merits of their poems, one must admit the doctors have not overlooked the entertainment principle. Yes, match the poem to the mood, of course, but also use the poem as a compensator, a means of covering up, neutralizing daily irritations—mesmerizing them out of apparent being. Even bad-poetry (doggerel) or, as Pope called it, "Prose run mad" is a gratifying pastime, for rhyme-making is fun.

The physician truly sees the poetry in life and often makes a stab at recording it. This is only natural, for as long as he lives and practices medicine, he has to face suffering, pain, disease, birth, and death. Boil this down and you find the physician covers every tendency discernible in life. The physician can and does become lyrical about what he knows, and in so doing he gives his work the vitality which is its fundamental excuse for being. The physician's mind comes to grips with concrete issues, and so he can contribute something toward the solution of the immediate problems of his period.

We can see it is no wonder at all that some physicians have the urge to put it down in verse and find it a pleasurable pastime and surcease from the cares and worries of the day. An Alabama physician, Dr. Samuel Minturn Peck, brings this thought out in the verse from his little volume *Cap and Bells*:

AMONG MY BOOKS

Among my books—what rest is there

From wasting woes! what balm for care!

If ills appall or clouds hang low
And drooping dim the fleeting show,
I revel still in visions rare.
At will I breathe the classic air,
The wanderings of Ulysses share;
Or see the plume of Bayard flow

Among my books.

* * *

Whatever face the world may wear—

If Lillian has no smile to spare,
For others let her beauty blow,
Such favors I can well forego;
Perchance forget the frowning fair

Among my books.

And reading his verse you can see that the good Doctor Peck isn't talking about medical technical books. As Carlyle said, "The true University these days is a collection of books;" and Disraeli said, "Volumes I prize above my dukedom."



Speaking of a play on words (and were we?), Thomas R. Henry, Science Editor of the *Washington Star* reports an extensive study of the physique of several hundred college girls conducted by the American Society of Physical Anthropology. The doctors have decided that girls have less physical stamina than men because their bodies are more likely to be out of balance. They used a scale which already had been applied to college men. The body was divided into five zones and each zone was classified for "soft-roundness," "muscular solidarity," and "delicacy." In men it had been found that,

THE DOCTOR IN LITERATURE

when one zone rated high in one of these qualities, all the others were likely to rate high. For example, muscular solidarity of chest would probably be accompanied by muscular solidarity of legs and arms.

With the girls this was found much less likely to hold. Whereas one part of the body might rate high in muscular solidarity, other parts might be character-

ized chiefly by soft roundness. In spite of this poor showing for girls, the two anthropologists called attention to the fact that normal young women show a considerable development of three muscles. One of these connects the head, neck, and shoulders, another is on the outer thigh, and a third is on the inner leg. The development of these muscles contributes to the dis-

tinctive appearance of the female outline!

* * *

And so, as we begin Anno Domini Nineteen Hundred and Forty Seven, we like to think it was O. Henry who said, "Life is made up of sobs, sniffles and smiles with sniffles predominant."

M. L. McD.

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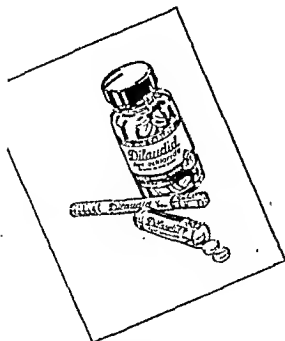
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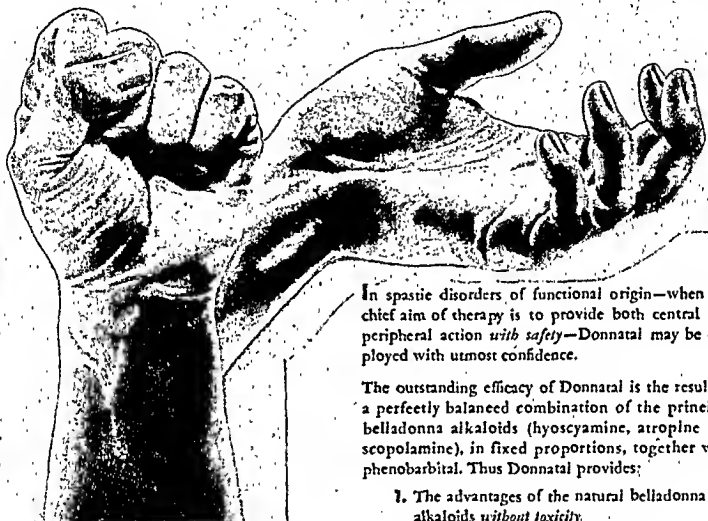
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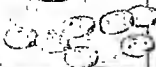
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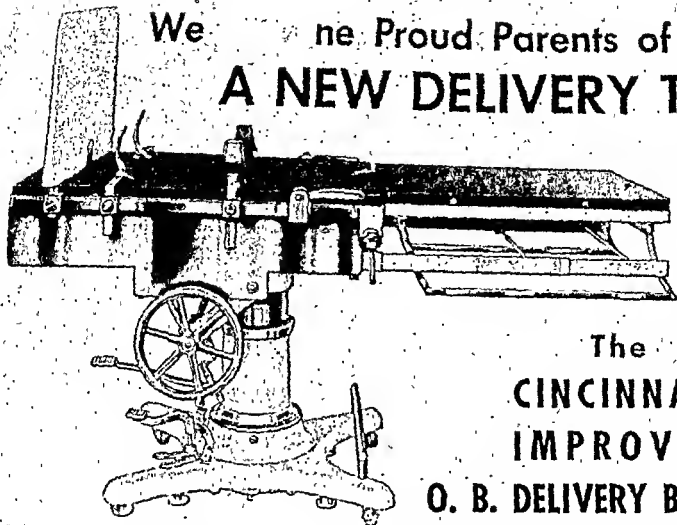
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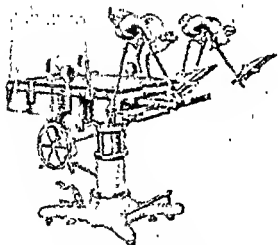


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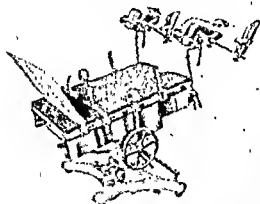


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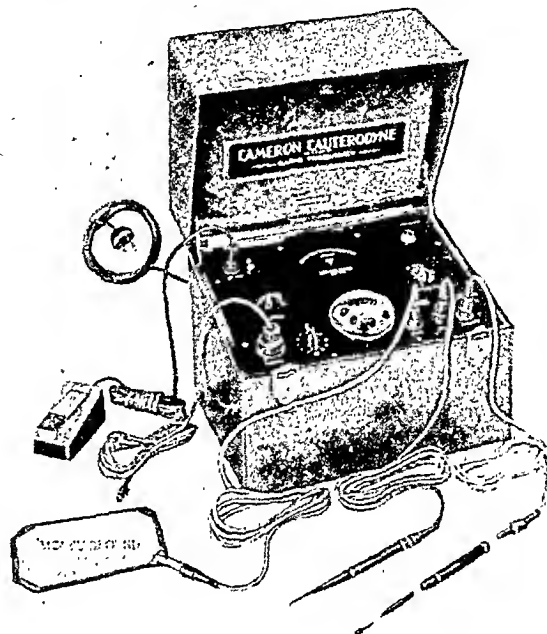
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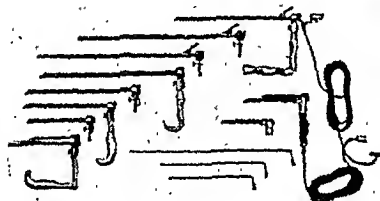
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MAY 1947

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Drew W. Luten, M. D., ASSOCIATE PROFESSOR
OF CLINICAL MEDICINE, WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE, ST. LOUIS

TREATMENT OF ANTERIOR POLIOMYELITIS

William T. Green, M. D., ASSISTANT
PROFESSOR OF ORTHOPEDIC SURGERY,
HARVARD MEDICAL SCHOOL, BOSTON

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Waltman Walters, M. D., PROFESSOR OF
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Diagnostic Clinics

DIAGNOSIS OF ACTIVITY IN PULMONARY
TUBERCULOSIS

Raymond C. McKay, M. D., ASSOCIATE
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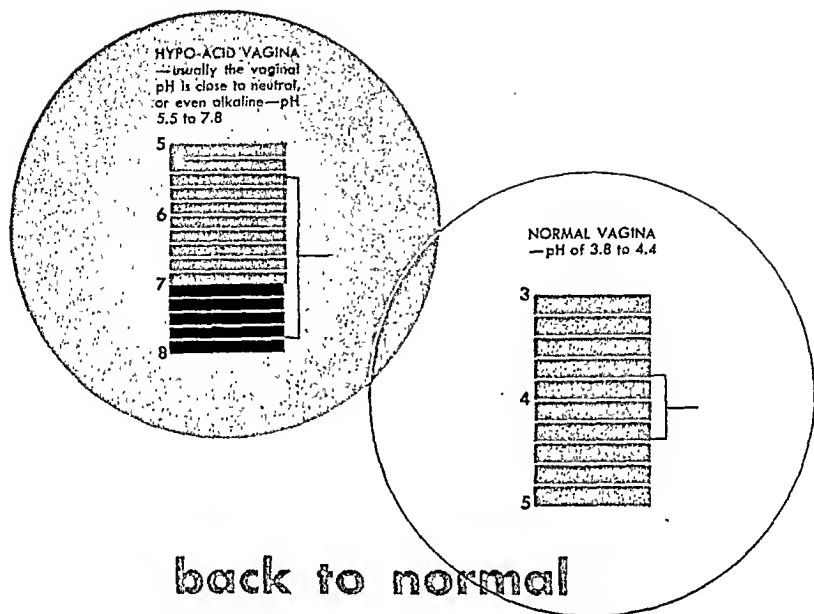


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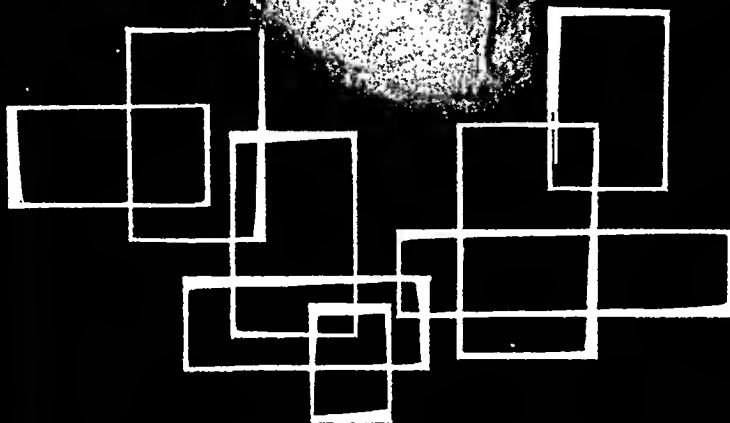
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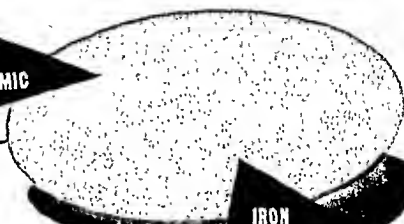
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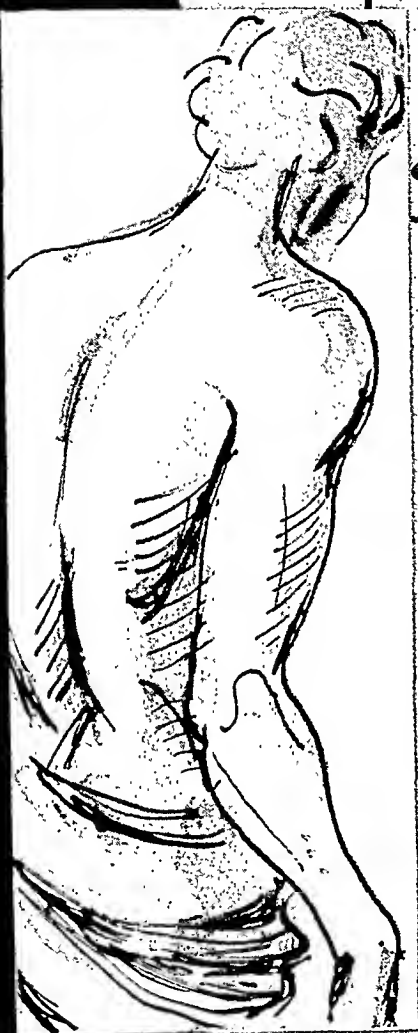
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¹ I. Sevringhaus, E. L., Am. J. Obstet. & Gyn., 37:913, 1939

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The Clinical Course of Coronary Disease

DREW W. LUTEN*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

THIS discussion of coronary disease will be restricted to atherosclerosis, the group which comprises by far the greatest number of cases. Disturbances of coronary function resulting from sclerosis will be reviewed, and the varied and varying course of clinical coronary disease will be outlined. Some essential features of the anatomy and physiology of the coronary circulation, both normal and pathological, first may well be reviewed.

ANATOMY AND PHYSIOLOGY

In later years it has become well known that there is a rich network of anastomoses which runs throughout the muscle and connects terminals not only from neighboring small branches, but even from the right and the left coronary. It now appears that, instead of increasing the number in later years, nature laid them down to begin with—many tiny communicating filaments with little to do but ready when called on. If there is any interference with arterial flow in one locality, an inflow of blood

is sent from less obstructed territory through these subsidiary channels, which enlarge with use.

TWO IMPORTANT FACTORS IN THE REGULATION OF CORONARY FLOW

In order to meet changing requirements, the amount of blood supplying the normal heart muscle must be subject to variation. For the most part, this variation in coronary flow is accomplished by change in coronary pressure, which automatically follows any change in the mean level of blood pressure. This automatic change in coronary pressure operates irrespective of any change in the caliber of the vessels; but vessel caliber also may change and thus may influence coronary flow. There is, however, an overall mechanism, beautifully and delicately balanced, which tends to guard against too great variation in vessel size. A constant stream of sympathetic stimuli to the coronary arteries tends to keep them in a mild state of tonic dilatation. Normally this dilatation overbalances the stimuli of the vagi, which tend to cause constriction and reduction of flow. Thus, tonic dilatation minimizes the effect of reflex vagal constriction, which might arise from pain, for example, and which, if strong, might otherwise suddenly lower coronary flow.

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NOTE: Read before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio, October 15 to 16, 1946.

CORONARY INSUFFICIENCY AND SCLEROSIS

The term "coronary insufficiency" implies that, under given conditions, the coronary flow is inadequate for normal needs. The insufficiency may be relative; that is, if the flow is augmented—by exercise, for example—and it still is not great enough for the yet greater requirement of the moment, *relative* insufficiency exists. If actual diminution of flow—from narrowing of an artery, for example—produces the insufficiency, it is termed *absolute*.

A sclerotic vessel may contribute to insufficiency in several ways. It may be unable to dilate normally in response to normal sympathetic stimuli, thus promoting relative insufficiency. Sclerosis also may narrow the caliber and thus cause absolute diminution or even stoppage of flow. It is evident that hypernormal constrictor stimuli (vagal) also could produce absolute insufficiency. This might take place in certain areas even in the presence of considerable sclerosis in other locations. Under such conditions, indeed, the consequences of constriction might even be especially serious.

LATENT CORONARY DISEASE

In the normal coronary circulation, as in the function of other organs, nature rarely calls regularly for full capacity. A considerable restriction of coronary flow may occur without impairment of usual function. Sclerosis of fairly large extent may be present without symptoms. The very effect of local insufficiency tends to develop collaterals which arise in more fortunate areas.

Postmortem studies show that in a very large percentage of adults past middle age who died of causes unrelated to the heart and who had no history of cardiac symptoms, coronary sclerosis of greater or less extent was present. In these people, nature's reserves sufficed. No important effects of restricted flow ensued. In coronary sclerosis uncomplicated by hypertension, congestive failure, valvular disease, or other cardiac lesion, there is little if any enlargement of the heart, no murmur, and in

many instances no abnormality of the electrocardiogram. In these cases of latent coronary disease, diagnosis commonly waits on post-mortem examination.

CLINICAL CORONARY DISEASE

Coronary sclerosis, however, may restrict blood flow below the level necessary for proper muscle function. Coronary insufficiency thus produced may last for brief intervals or for long periods. Angina, myocardial infarction, and congestive heart failure may result.

In reviewing separately these various manifestations of clinical coronary disease, I shall ask you to note the fact that they divide themselves primarily into two rather separate and distinct groups, and that the symptoms of the one are quite different from the symptoms of the other; they are diverse. There is indeed very strong evidence that the symptoms associated with the one group are in fact more or less incompatible with the situation existing in the other. In one group there are evidences of acute disturbance related particularly to the coronary arteries; this occurs in cases of angina and of acute infarction. In the other group there are evidences of chronic impairment of the heart muscle; such are cases of congestive failure. In the acute arterial cases the characteristic evidences of congestive failure regularly are lacking; in the more chronic muscular cases with congestive failure, the clinical manifestations of acute arterial disturbance regularly are in abeyance. The patient with acute coronary disturbance may be destined ultimately to travel the other road, but rarely does he go both ways at once.

In like manner, the patient with primary muscular insufficiency commonly exhibits none of the evidences of acute coronary disturbance. The explanation of this rarity of angina and of infarction in primary congestive failure is not entirely complete. Change in blood volume might be the differential. Congestion of the coronary veins in congestive failure has been thought to explain it. Muscle space may hold the answer. The patient with uncompli-

ated angina shows no cardiac enlargement, whereas enlargement regularly accompanies congestive failure. The following consideration appears to bear upon the problem. In congestive failure the elements of ventricular muscle are less compact; they occupy more space, and consequently they may be expected to allow more room for coronary flow. Conversely, as the dilated muscle improves, the coronary bed may be relatively encroached upon. Whatever the explanation, angina does not give the signs and symptoms of congestive failure; during congestive failure the occurrence of angina or of infarction is rare.

ANGINA

Temporary myocardial ischemia, relative or absolute, commonly produces a more or less characteristic sensation. It is usually substernal, but the location may be confined to one or both arms, the elbow, the left or right chest, the back, or the epigastrium.

Characteristically it occurs with exercise—especially in the early morning, more regularly after a meal, and particularly after the early morning meal. It often occurs with emotion, after a breath of cold air, sometimes on taking food, or on arising from a sitting posture. It may occur in the night or on arising. More rarely—and particularly in relatively serious cases—it may occur while sitting, particularly after eating, and in association with excitement or other “tension.” Usually, but not invariably, it yields readily to nitroglycerin 1/200 grain or less, in the mouth. In many instances the patient refuses to designate the sensation as pain, and objects to that term. In others, the pain is excruciating. He often refers to it as “shortness of breath,” but careful questioning nearly always reveals that it is not associated with increase in number or depth of respiratory movements. The pain instead may seem to shut off his breath or “to take his breath away,” not to increase his breathing.

Cessation of effort, subsidence of emotion, belching of gas, or removal of other precipitating factors, regularly is soon followed by dis-

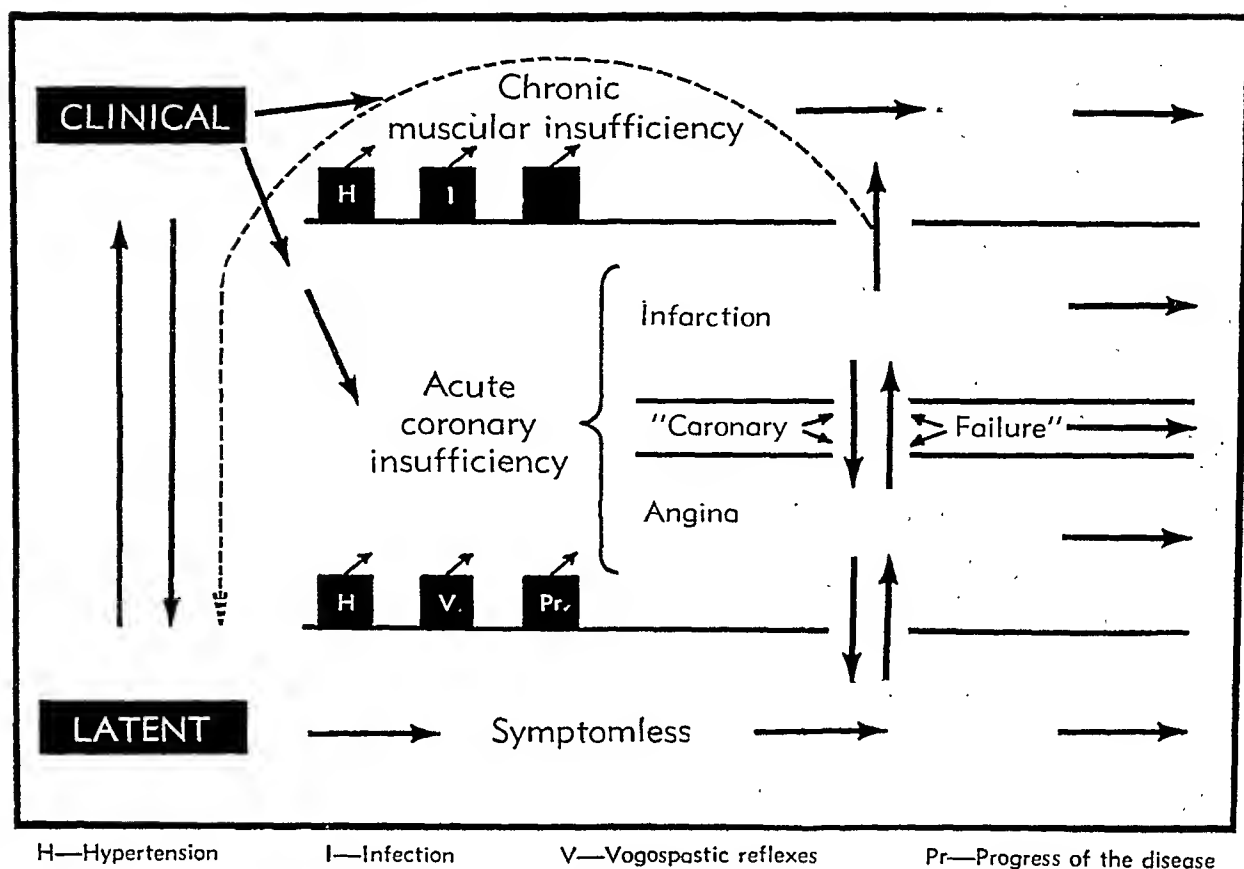
appearance of the attack. In most instances the duration is measured by minutes. Chest pain that lasts longer than a matter of minutes should be regarded as due to causes other than coronary disease or to some other disturbances of the coronary circulation mentioned below.

Angina occurs particularly in individuals who take responsibility seriously, especially in those working under tension. It is often associated with hypertension and with digestive disorders, which appear to be contributory factors.

The term “angina of effort” often carries a wrong implication, and it would be better to use only the word “angina.” In a large proportion of patients with angina, it is true that the occurrence of pain appears to depend upon relative coronary insufficiency induced by physical activity. In many other cases the circumstances of onset strongly indicate that the insufficiency is absolute, resulting from reflex nervous effects which reduce the coronary flow, there being at the moment no particular need for increase in blood. It would be difficult otherwise to explain the occurrence of anginal pain from a breath of cold air, or some of those cases in which the pain follows the mere swallowing of food. Long ago it was well known that angina occurs particularly after a meal. The frequent association of angina with various disorders of the stomach, gallbladder, duodenum, and colon gives strong clinical evidence that in some cases a hypersensitive or overdeveloped constrictor reflex (vagal) may be responsible for the attack, in patients with coronary disease, by reducing still further the coronary flow which was near the critical level because of sclerosis. Certain clinical experiments support this view. Attacks of angina have been induced by mechanical distension of the esophagus or of the stomach.

Gilbert and his co-workers have furnished very important experimental evidence, both from patients and from the animal laboratory, that anginal attacks may be induced by vagal stimulation. In producing angina by administering a low oxygen mixture to susceptible patients, and noting the time that was required to

The Clinical Course of Coronary Disease



In the figure above, the varying course of coronary disease is graphed. It will be noted that cases with symptoms may become symptomless, and *vice versa*. Or symptoms may change, the clinical cases tending to be classified into rather distinct groups. Some of the factors which may influence the course of the disease are indicated.

produce any pain, they found that the attack came at an earlier moment in the experiment if the patient had had a full meal first, but that this earlier appearance of pain did not occur if atropine had previously been administered.

These experimental results, as well as many of the longstanding clinical observations, are easily explainable as due to reflex vagal constriction, hardly on any other basis. The view is held by some that constriction of the coronaries may result from irritation of the vagus center and may be strong enough on occasion to produce serious ischemic effects in the myocardium even in the absence of notable sclerosis of the arteries. Although the evidence in favor of

vagal effects in precipitating attacks in certain cases of angina is impressive and should always be kept in mind, the evidence also is overwhelming at present that coronary disease of greater or less extent also exists in almost if not in all cases, except in those associated with thyroid disease, anemia, or in other easily explainable situations.

In many patients attacks of angina constitute the only demonstrable effect of coronary disease. In such cases obviously the diagnosis can be made only from the history, but in most instances this is sufficient. Evaluation of the history may present considerable difficulty, but as a rule the characteristic features can be elicited

or excluded by painstaking and detailed questioning.

Course—Coronary disease of extent sufficient to produce angina is a serious matter. Sudden death may occur. Complete occlusion with or without myocardial infarction may ensue. Congestive failure may follow. In many instances the development of collaterals, the avoidance of precipitating factors, and the relief of accompanying disturbances may result in temporary or permanent cessation of attacks, the disease then becoming latent. In many cases proper attention to abdominal symptoms yields valuable results. And equally if not more important, the patient should have the confident assurance from his doctor that nature, continually at work to develop an adequate collateral circulation, may count him among her successes.

CORONARY OCCLUSION AND MYOCARDIAL INFARCTION

Acute occlusion of a diseased coronary artery commonly implies thrombosis but it may occur in other ways. Atheromatous material may block it. If the closure develops slowly, giving time for the development of adequate collaterals, the ischemic area may not undergo infarction. Blumgart has shown that many cases of angina originate in this manner. Infarction itself may not imply complete closure. Its characteristic clinical picture depends not on the method of origin but on the infarct itself.

Occurrence—The circumstances attending the initial symptoms of acute infarction usually present certain differences from those attending the occurrence of angina, but they commonly show certain similarities as well. Angina occurs so characteristically with effort that it is commonly called "angina of effort." The initial evidences of thrombosis, on the other hand, are relatively rare with effort. Indeed, a certain amount of physical activity may tend to prevent thrombosis. Activity promotes coronary flow and thus opposes thrombus formation even though the increased flow may yet be inadequate (and thus induce angina). There has been much discussion as to the precise relation-

ship of infarction to physical activity. So far as concerns those cases resulting primarily from thrombosis, there would appear to be little room for argument. Although exceptions are well recognized, the symptoms of infarction from thrombosis characteristically begin when the patient is relatively quiet, particularly during sleep, when blood pressure is lowest and coronary flow consequently diminished. Angina at night, indeed, may result from the same mechanism. In patients with coronary sclerosis, circumstances which lower blood pressure on occasion may therefore carry considerable risk of inducing thrombosis.

THERE is considerable evidence of strong reflex vagus stimulation in many cases of infarction as well as of angina. The association of infarction with disorders of the gallbladder, stomach, and other abdominal viscera has long been recognized. Perhaps the commonest effect on rhythm in acute infarction is sinus arrhythmia with slowing of the rate. Some of this vagus stimulation well may result from the infarction itself, but evidence of a causal relationship, by restriction of coronary flow, often is impressive. By avoiding such reflex nervous effects the risks of infarction as well as of angina obviously may be lessened. Evidence has been advanced to show that, in acute occlusion, reflex vagus effects overflow to neighboring coronary branches, thus augmenting the ischemic effects and tending to enlarge the affected area. Experimentally this vagal constriction is counteracted by atropine. Such considerations make clear the rationale of giving atropine early in acute infarction.

The clinical features of myocardial infarction vary in occurrence and also in intensity. Unlike angina, the pain, unless relieved, usually is measured by hours. It may diminish or disappear and then recur without apparent exciting cause. Nitroglycerin usually has little effect. If the diagnosis is clear, it should not be used. Often there is dyspnea, occasionally as the main presenting symptom. The patient may be in shock. Syncope is not unusual. The attack may

be characterized principally by dizziness. Upon occasion there is no pain. Almost always fever develops. The blood pressure may even be elevated for a time, but in most cases it falls sooner or later. Usually there occur leukocytosis, increased sedimentation rate, and electrocardiographic changes which commonly, but not invariably, are characteristic. Pericardial friction may be noted.

The myocardial effects of acute infarction are more profound than in most instances of angina. As a rule, however, the initial circulatory effects do not indicate muscular insufficiency with congestive failure. In some instances acute muscular failure occurs; and in others chronic congestive failure follows. The heart muscle in acute infarction, however, is involved in a process altogether different from that which obtains in chronic muscular insufficiency.

Course—It is widely recognized that death may occur early in infarction, but it is also now well known that the dire forebodings of some ten or fifteen years ago in very many cases have had to be revised. If the patient is in good condition a week or two following his attack, his chances for returning to activity are good. Embolism or other serious event may still supervene, but in general, the first few weeks give excellent prognostic implications. In many instances recovery is complete, and the patient lives out his expectancy with no cardiac symptoms. Subsequent attacks may occur, which may be more or less severe than the first. I have observed some cases in which even the third attack has left the patient well able to look after his work with little or no clinical evidence of heart disease.

In other instances invalidism results. The patient may be in a chronic state of coronary insufficiency with attendant symptoms. Congestive heart failure may ensue. Even so, complete recovery without need for digitalis may take place.

CORONARY INSUFFICIENCY

In many instances of acute coronary insufficiency, the clinical distinction between angina

and infarction is not as clear-cut as may have been indicated. The pain may last for long periods and may recur frequently with little or no apparent provocation; the patient evidently is quite ill, even though the criteria of infarction are absent. In some instances infarction supervenes; in others the pains subside and the patient improves without clinical infarction. Blumgart has suggested for such cases the designation "coronary failure." Others have suggested the term "impending" occlusion or infarction. The term "coronary insufficiency" has been proposed to separate such cases from other better classified instances of insufficient coronary flow. Whatever name may be used, it is essential to recognize the fact that such patients need special care and observation. Even though the situation usually is critical, in many of these, as in other instances of coronary insufficiency, the development of collaterals relieves the situation, and the patient reaches a high level of activity again with or without angina.

CONGESTIVE FAILURE

In many individuals coronary disease is an important factor in the development of congestive heart failure. The precise mechanism in the evolution of failure in such cases is not entirely clear. For certainly in many cases there is no exact parallel between the degree of coronary sclerosis and the presence or absence of congestive failure. According to Clawson, sclerosis tends to prevent hypertrophy. Whether sclerosis alone ultimately may induce congestive failure, without infarction and without other accessory factors, might be difficult of proof. In most instances of coronary disease hypertension also is present to put added strain upon the heart. Often infection appears to be significant. However, restriction of coronary flow itself, existing over a long period of time, must also be a large factor in myocardial insufficiency, especially if the impoverished muscle is subjected to undue strain. Although coronary disease per se tends to prevent enlargement, failing heart muscle regularly undergoes hypertrophy and dilatation whatever may be the underlying factors in the

failure. Usually the left ventricle is the first to show impairment of function, the presenting evidences being congestion of the lungs with breathlessness.

Course—As a rule, the course of congestive failure in patients with coronary disease is not particularly different from that in other patients. Precise differentiation of all contributory causes may be quite difficult. On occasion, with control of accessory causes, proper therapy may enable the muscle again to function well for an indefinite time.

SUMMARY

Coronary disease may exist without apparent effect on muscle function, or, under various circumstances, it may result in failure of the muscle to perform its work in a normal manner. This failure to work properly may be characterized by diminution in pumping capacity, i.e., "congestive failure"; or it may be manifested by pain, i. e., "anginal failure." Rarely does the patient experience both types at once. There appears to be an incompatibility between them.

The coronary patient with chronic congestive

failure commonly is one who has undergone long-standing restriction of coronary flow, to which usually has been added some important contributory factor. In most instances the course is not conspicuously different from that observed in other cases of congestive heart failure. Evidences of acute coronary insufficiency rarely are present.

The patient with anginal failure is one who has experienced an acute coronary insufficiency. There is much evidence that this acute insufficiency in some cases may be superinduced by hypersensitive vagal influences. It may take the form of angina or of myocardial infarction. From either of these acute types the patient's course may lead to the other. Or, especially in cases of infarction, it may lead to chronic muscular insufficiency.

Along with restriction of coronary flow, there is a progressive development of the intercommunicating collaterals. In many cases of acute coronary insufficiency this collateral circulation increases to such an extent that again the circulation is adequate and the patient no longer experiences the symptoms of insufficiency.

ALLOXAN

One of the most interesting recent developments in the field of diabetes has been the discovery of the selective destructive action of alloxan for the islets cells of the pancreas. Animals into which alloxan is injected develop a diabetes which in many notable respects resembles human diabetes.

But aside from its value in the study of diabetes, alloxan has been considered as a possible agent in the treatment of persons suffering from hyperinsulinism caused by islet cell carcinoma. A small number of investigators have used alloxan for this purpose. Results have been disappointing, for it has been found that injection of alloxan produces severe liver necrosis and fatal toxic reactions. Though the normal islets of Langerhans are destroyed, islet cell adenomas appear resistant to the action of alloxan. Because of its extreme toxicity, its use in human beings is not advised.

Present Methods in the Treatment of Anterior Poliomyelitis

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INFANTILE paralysis is a disease due to a neurotropic virus, the effects of which are most variable. The acute febrile part of the illness, at the start, may be nonspecific in type, but it soon exhibits symptoms referable to the central nervous system. These include headache, irritability, muscle sensitivity, muscle spasm, and paralysis. Paralysis may or may not occur. If present, it tends to be patchy in distribution with regional localizations. It may be widely distributed and almost complete. The individual muscles may be affected in any degree from barely detectable weakness to complete paralysis. The sensitivity and spasm are self-limited and, in most cases, of relatively brief duration. The spasm may range from barely perceptible to severe. It may persist for months but ordinarily it lasts only a few weeks.

Prognosis as to recovery depends more on the degree of original involvement than upon any other factor. Death, if it occurs, is usually due directly or indirectly to bulbar involvement or to paralysis of the muscles of respiration. Since the disease presents a combination of paralysis, sensitivity, and spasm, it is particularly deforming and since deformities with shortened muscle become fixed with fibrous and fascial contractures, if they are allowed to

develop, they tend to be maintained. In children, secondary growth disturbances produce still further abnormality. Once the acute illness is over, the picture of paralysis is always one of improvement. Some muscles may remain completely paralyzed, others recover completely, and there are all variants in between. The total picture, however, is that of improvement.

The degree of recovery which will occur cannot be estimated accurately in the early stages of the disease. The greater the degree of paralysis and the more extensive its regional distribution, the worse the prognosis.

STAGES OF DISEASE

The course of the disease is such that it seemed wise to Lovett, years ago, to subdivide it into stages, and such a division, considerably modified, is desirable in our consideration of treatment.

Now this is the disease about which there is so much confusion, so many claims and so many counterclaims. Why is this?

The nature of the disease itself is a large contributing factor. There is no way in the initial stage before paralysis occurs to estimate the degree of paralytic involvement which will ensue, nor in fact to determine accurately in the early stage of paralysis the degree of recovery which may occur. It is natural to ascribe the results attained to whatever treatment is

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followed. Even if no treatment is given, a very considerable percentage of patients seen in the early stage will either have no recognizable paralysis or very little and complete recovery. This becomes of greater significance when considered in relation to the great variation in severity of the disease, not only in individual cases but in particular epidemics.

TABLE I

STAGES OF DISEASE

- I. Acute Stage—Period of acute febrile illness.
 - A. Preparalytic phase
 1. Period of acute illness before paralysis is discernible.
 - B. Paralytic phase
 1. Period from onset of paralysis to end of febrile stage.
- II. Convalescent Stage or Stage of Recovery—Period of convalescence when recovery of muscles may occur. Arbitrarily, it may be said to terminate 16 months after the onset.
 - A. Sensitive phase
 1. Period when muscle sensitivity and spasm are present.
 - B. A-sensitive phase
 1. Period after sensitivity and spasm have subsided.
- III. Chronic Stage—Period starting with end of Convalescent Stage.

FOR EXAMPLE, if all the cases seen later than the earliest stage of the disease are discarded from the series which is reported, on the basis that the treatment is not effective unless it is given from the start, the recovery on a percentage basis will be high, since many non-paralytic cases or cases with the mildest involvement will be included in the series.

I cannot help but emphasize the natural recovery which occurs in infantile paralysis. I believe that I can best illustrate this by a quotation from a textbook published in 1894. In the chapter on anterior poliomyelitis was this statement: "If genital irritation exists and phimosis be suspected as the cause, circumcision will be indicated as soon as the more acute symptoms have subsided, and may be followed



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by the speedy amelioration of the paralysis; but the writer now has a boy under his care in whom circumcision, undertaken by another surgeon after the attack, had no effect whatever on the paralysis."² In other words, whatever is done many patients get well. I cannot pass without affirming that treatment has much to do with the outcome, but certainly spontaneous recovery must be considered in evaluating results that are obtained.

Upon this setting, we have had extravagant claims and promises regarding the results of particular treatments. Add to this the intense public interest in this disease, which cripples children, together with publicity of a type and amount never before existing in the history of medicine, and there is little wonder that confusion has existed.

HISTORICAL BACKGROUND OF TREATMENT

It is well to recall some features of the historical background of the treatment of the disease. It appears that the late Robert Lovett, formerly chief of the Orthopedic Service at

our hospital, had as much to do as anyone with the placing of the treatment of the disease upon a good foundation. His activities were confined to the first quarter of this century.

He subdivided the disease into stages, pointing out that the treatment varies as to the stage. He described the acute stage as persisting until muscle tenderness disappears. He emphasized that flaccid paralysis, due to involvement of the anterior horn cells, was the outstanding feature of the disease, although affirming the work of Peabody, Draper, and Dochez that other parts of the central nervous system were affected.³ He stressed the sensitivity of the muscles in the acute stage, their rigidity, and the deforming tendencies. Spasm in muscles of the neck, the hamstring muscles, and the back were described as an important diagnostic feature. He emphasized that deformities must be prevented and advocated the use of splints, when indicated for this purpose. He recommended rest and the support of parts in the acute stage as well as avoidance of massage and strenuous physical therapeutic measures which he felt prolonged the period of sensitivity. He advocated warm baths and hot fomentations for sensitive muscles.

In the convalescent stage, active exercises directed toward the function of specific muscles were performed. A technique of muscle examination was evolved, classifying the individual muscles as to strength into six grades—zero, trace, poor, fair, good, and normal.^{1,4} This grading is the method in current use today. At this stage, too, emphasis was placed on the prevention and correction of deformity and splints were used as necessary.

The patient was gotten up after not too long a period as he believed that the upright position was desirable quite early in the convalescent phase. Braces were used as indicated. It was stated that if a patient cannot stand or walk unaided, or stands or walks in a position of deformity, as with a hyper-extended knee, the use of a brace was desirable. He emphasized the importance of muscle imbalance in producing deformity.

In the chronic stage the concern was to develop and maintain as satisfactory function as possible.

Since this original outline by Lovett, evolutionary changes have occurred. The late Arthur T. Legg, who succeeded Lovett, advocated the use of hot packs during the sensitive stage.⁴ Guided active exercises were started at an earlier period in the disease. Underwater exercises came into greater use. The importance of early passive motion to prevent stiffness was advocated.

Now there were others who recommended a greater degree of immobilization and exercises involving limited arcs of motion, and still others who felt that treatment was of little help.

Upon this setting comes the treatment developed by Sister Kenny, but which itself is going through an evolutionary phase. This treatment was proposed as a radical departure from previous concepts and was claimed to be revolutionary in its results.

THE THREE cardinal features of the disease as proposed by Sister Kenny are (1) muscle spasm: "the affected muscles are the muscles in spasm," (2) incoordination, and (3) mental alienation.⁵

Pohl asserts that: "Spasm of muscle is the earliest, most common and most damaging finding affecting the muscles in acute anterior poliomyelitis." Paralysis due to destruction of anterior horn cells is recognized as occurring, but it is held that "paralysis proves after all to be a minor consideration in most cases of infantile paralysis." The treatment proposed by Sister Kenny is directed toward the muscle spasm, incoordination, and mental alienation. Great effort is directed toward minimizing the spasm with the idea that the course of the disease will be greatly influenced.

Mental alienation is a term used to describe a condition in which there is an inability to produce a voluntary purposeful movement in spite of the fact that the nerve paths to the

muscle are intact, a "physiologic or psychologic" block. The majority of the muscles described as alienated by Sister Kenny are those which I would evaluate as exhibiting either a flaccid paralysis or paresis.

Involved in the technique of treatment are the use of hot packs on a regular schedule by a particular method, the avoidance of underwater therapy, as well as splints and casts, which are ascribed as being harmful. However, attention is given to the position of the parts, particularly through nursing care and the use of a footboard. The purpose of the footboard is allegedly not to hold the foot but to stimulate proprioceptive reflexes. Muscle education is started at a relatively early stage; its features will not be outlined here. The techniques in many respects seem to be similar to those which are in use in certain of the so-called orthodox methods, although they are described as being performed for a different purpose and to be based upon a different concept of the disease. Sister Kenny does not do a muscle examination, that is, does not evaluate the power of the individual muscles, but does what is called a muscle analysis, which primarily is a recording of the spasm present.

The respirator is described as not having a place in treatment. Braces are said not to be necessary and deformities such as scoliosis are stated not to occur.

Others recently have recommended the use of curare, intramuscularly, together with strenuous manipulations and early activity, encouraging any motion which moves the part. This technique has been described as producing superior results. Other drugs are advocated as having particular virtue. What of all this?

PATHOLOGY

LET US first consider the pathology of the disease. The histologic changes in the central nervous system are quite widespread. Not only is the spinal cord involved, but various portions of the brain, and even the posterior ganglia. However, the most destructive action

occurs in the gray matter of the anterior horn and in adjacent cellular areas.

The pathological changes seem to be due primarily to the effects of the virus upon the neuron with the edema, and cellular infiltration representing secondary phenomena.

The weakness of a muscle is in turn, due to loss of neuromuscular units, that is, loss of those muscle fibers innervated by the involved neurons. For example, a muscle classified as "trace" has enough units working to provide a palpable contraction but not enough to move the part.

The changes in the anterior horn cells vary from minimal abnormality to complete destruction of the neuron. By indirect evidence it seems likely that this variability of histological change is an index of the functional action of the neurons and of their recovery. To elaborate, cells may be affected in minimal fashion so as temporarily to disturb axonal conduction and their loss of function is of brief duration. They may be affected more severely with a prolonged afunctional period which exists until rather extensive regeneration occurs. Or they may be completely destroyed with no possibility of recovery.

The pathological process responsible for muscle spasm and sensitivity is still unknown. In 1916 Lovett suggested that the sensitivity might arise from the involvement of the posterior ganglia. Other suggestions have been made recently. Kabat and Knapp have suggested that it is due to the involvement of the internuncial neurons which are closely associated geographically with the anterior horn cells.⁶ This is a possibility. There are others who believe that the sensitivity and spasm arise as a peripheral mechanism. Whatever the cause, the spasm present is not spasticity of the type seen in cerebral palsy and is or closely resembles reflex muscle spasm. Clinically, it has very much more in common with the type of muscle spasm that one sees with painful inflammatory lesions, such as the spasm of the abdominal muscles occurring with peritonitis or the spasm of the hamstring muscles as a protective mechanism for an infected knee joint.

For the present, we consider paralysis and spasm as separate features of the disease. They both contribute to the disability, yet spasm is a very secondary factor in its relation to the permanent disability. It is certainly not the serious feature of the disease. Spasm without paralysis is an inconsequential thing. It produces discomfort and is a factor in producing deformities in the acute stage, when combined with paralysis. Eradication of the spasm at an early stage will not prevent the paralysis, which is the main factor in permanent disability. Lessening the spasm does assist in the correction of deforming tendencies, makes the patient more comfortable, and in turn allows muscle training to be instituted at an earlier stage.

It is appreciated that in a disease which is so widespread in the central nervous system, factors other than those appreciated at this time must contribute to the picture of anterior poliomyelitis, but until further clarification in the fields of neuropathology occurs, many concepts must be theoretical. It is a field for further investigation.

PRINCIPLES OF MUSCLE FUNCTION AS RELATED TO TREATMENT

I SHOULD like to enumerate some principles of muscle function and pathologic physiology in relation to the abnormalities which occur in infantile paralysis, at the same time illustrating their relation to principles of therapy.

1. Muscular action is inhibited by pain, sensitivity, and spasm.

2. Muscles in spasm, particularly in the presence of the muscle imbalance, produce deformity.

3. Muscles maintained for significantly long periods in a position of shortening develop myostatic contracture with fixed deformity and fibrous and facial contractures.

4. Muscles working against a deformity are inhibited in their recovery and in fact may lose power.

Let us conclude here that, in infantile paralysis, parts must not be left in the positions of

deformity. Deformities must be prevented and the deforming tendencies corrected. Nursing care should emphasize attention to position, but if the desired position cannot be maintained, splints and casts are indicated for a variable period each day. Ranges of motion should be developed without inducing increased pain and spasm. Measures to decrease spasm are in order; hot packs judiciously used are helpful.

Let us consider other principles.

1. Movement of the various parts involve a complex motor pattern with which we are born and which is essentially a reflex pattern. If a muscle is left out of a particular pattern for a sufficient period, as for example from an inability to contract due to denervation, it appears that it is possible for the muscle to recover its innervation and its potentiality of contracting without resuming its activity. To make this principle directly applicable, if when a muscle is paralyzed, other muscles are allowed to substitute at all times for the action of the involved muscle, this muscle may recover its possibility of contraction, but be left out of the pattern of motion.

2. Most muscles, even those badly affected by infantile paralysis, have some neuromuscular units preserved, which act as "guiding contractile units."

The combination of these factors, namely, that muscles may be lost from the motor pattern and not resume their place even with potential ability to function, and the fact that guiding units remain in most affected muscles, is one of the important bases upon which the active exercise regimen during the convalescent stage is founded. Guided active exercises are developed avoiding substitute muscular actions and making sure that muscles which should function in the motion are the ones that do. If the patient cannot perform the motions, he is assisted. Abnormal patterns are to be avoided in the stage of recovery.

Certain other principles upon which the therapeutic regimen is based should be elaborated.

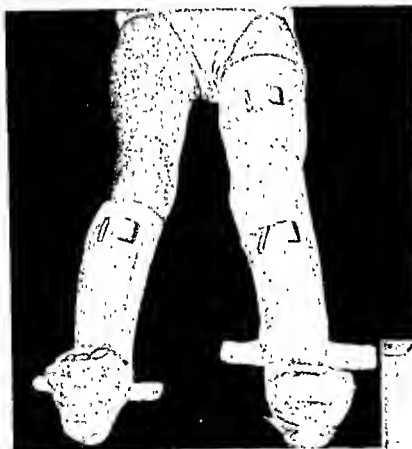


Figure 1. (Top) This illustrates marked muscle spasm in the back and in the hamstring muscles, preventing the child from going farther into the sitting position when the knees are held in extension. Spasm is an important diagnostic finding and is likewise a deforming factor.

Figure 2. (Left above) Bi-valved plaster splints, or splints of other material, are desirable in a certain percentage of cases to hold parts out of a deforming position. They are particularly useful to hold the feet and are usually used on a part-time basis. They do not interfere with other necessary therapy.



Figure 3. (Center right) Crutches are frequently desirable when walking is first started, provided the arms are normal.



Figure 4. (Lower right) Guided active motion directed toward the use of particular muscles. Muscle substitution is not allowed during the exercises of the convalescent phase.

TABLE II

MUSCLE EXAMINATION

Grading of Muscle	Definition
O	No palpable contraction of muscle.
Trace	Palpable contraction of muscle, but no motion of the part which the muscle should move.
Poor	Muscle moves the part through its range, but not against gravity.
Fair	Muscle will carry part through its range of motion against gravity, but not against added resistance.
Good	Muscle will lift part against gravity and added resistance.
Normal	Normal strength.

In practice, certain modified grades may be added:

Poor	A muscle which will move part, but not against gravity and not through a full range.
Fair	A muscle which will move part against gravity, but not through a full range.

1. Muscle examination, that is, the grading of the individual muscles, can be performed and charted with sufficient accuracy to evaluate the degree of paralytic involvement. Such examinations should be performed at regular intervals to record the degree of paralysis and return the progress of the affected muscles. They are a great help in outlining the active exercise regimen. There is no evidence whatever that such an examination is harmful if correctly done.

2. The ability to contract muscles is related to the performance of a motion, not to an isolated contraction of an individual muscle or the thought of apposition of origin to insertion. The position in which a muscle functions best, or where a contraction may be developed in a muscle, is variable and the position for exercises should be adapted to these variables, including gravity.

3. A normal full range of motion is the best exercise for a particular muscle, provided such degree of motion can be attained painlessly.

4. Muscles which are weak are inhibited in their recovery by overactivity and overwork. Further, if a muscle cannot carry out its function satisfactorily, it may lose power. The corollary to be added is that rest in proper amounts facilitates recovery. Rest and protection are two of the important factors in treatment.

5. If the activity and work of muscles are increased on a graduated scale, they hypertrophy. In turn, if a muscle which has lost neuromuscular units permanently is stimulated to function, made to work, yet not overworked, hypertrophy of residual muscle fibers occurs.

CERTAIN other rules affecting muscle function must be mentioned.

1. Severely affected muscles may resume function to carry out a particular simple motion, and yet not necessarily be returned to a synergistic function in more complex activities, that is, to the pattern of more complicated motions. Hence, in those significantly involved, supervision of the transition to more complicated activities such as walking is indicated.

2. Only a fraction of the power of any muscle is necessary for ordinary activity. This allows an individual to perform essentially normal activities with muscles which have some degree of residual weakness, particularly if no deformities exist and training has developed the maximal functional capacities.

3. Muscle imbalance tends to be a deforming factor, particularly during the growing period. The growth and contour of bony structures is affected by paralysis and abnormal function. In this connection the comment should be

made that long-continued supervision is indicated in growing individuals who have significant residue. Exercises both to maintain maximal function and strength, and to prevent deformities, are often indicated in the chronic stage.

4. Parts used in a normal position tend to retain such position, whereas those used in deformed positions with abnormal stresses tend to increase their deformity.

5. Complete prolonged immobilization seems to interfere with the functional recovery of muscles, but there is no evidence that support used intermittently and combined with physiologic exercise is harmful. Quite the contrary, in the care of a certain percentage of patients, it is most helpful. The use of splints or casts is desirable in many cases.

One other principle which is applicable to the chronic stage should be stressed.

Once the period of muscular recovery is passed, substitute muscular actions are desirable in many cases in which significant residual paralysis exists. Hence at this stage exercises should be concerned with developing maximal function, incorporating substitute muscular actions as indicated.

We have commented that if there is significant involvement when the patient starts to stand and walk, the gait should be carefully supervised, preventing abnormal attitudes and muscular substitution. However, in the chronic stage, substitute muscular action may be allowed and encouraged as indicated to produce that gait which is most effective and least unsightly.

Crutches may be indicated at the beginning

to remove abnormal stresses and facilitate the desired gait. They are rarely indicated as a permanent aid except in combination with braces. Braces may be needed to obviate deforming stresses as well as to allow practical locomotion. They do not represent a type of treatment but are used for specific indications.

COMMENTS

As we consider these principles, it becomes obvious that someone skilled in the care of the skeletal system should be concerned with care of the patient from the very start of the disease. In usual practice this means that the patient in the acute stage should be cared for by a team composed of a pediatrician or internist and an orthopedist. Infantile paralysis is not a purely medical problem, even in the early stage, and proper care of the involved areas prevents many complications which are difficult to correct. After the acute illness, the patient should be under orthopedic supervision with medical assistance as indicated.

It seemed wiser for us to emphasize the principles upon which treatment is based, rather than to discuss the details of technique and management. There has been no sudden revolutionary change in treatment. Improvements have come by an evolutionary process.

In conclusion I should like to emphasize that treatment must be based upon sound principles. We must be alert to improve our methods, but the new must be evaluated with scientific objectiveness. Faddism should have no place in the treatment of infantile paralysis.

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Developments in Surgery of the Upper Abdomen

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IN THE years before the war it was my custom to present to you some of the newer developments in the fields of surgery in which I am interested, with the idea of expressing my personal opinion of the procedures advocated in the light of my own experience and the experiences of my associates working in the same surgical fields. I shall endeavor to do so again on this occasion, but will confine my remarks to lesions of the upper part of the abdomen.

RESECTION OF THE VAGI NERVES

General considerations—First of all, I should like to consider the operation of resection of the vagi nerves which my colleagues and I prefer to call "gastric neurectomy." This procedure is not new. It has been used for many years in the study of the effects of division of these nerves on gastro-intestinal motility and gastric secretion. Dragstedt has called attention to the value of the procedure in the treat-

ment of gastric and duodenal ulcers, basing the rationale of the operation on the thesis that "the excessive secretory response of gastric glands in ulcer patients was probably due to an increased secretory tonus or irritability of the vagus nerves," and he has recently reported the results of this operation on 54 patients treated in the past three years. Fifteen of the patients required gastro-enterostomy either at the time of section of the vagi nerves, or subsequently because cicatricial pyloric stenosis had produced duodenal obstruction, contributed to in great part by the profound depression of the tonus and motility of the stomach which occurred after the operation. In determining the results of the operative procedure, Dragstedt has based his opinion on (1) the disappearance of the symptoms of ulcer, (2) the disappearance of the crater or niche of the ulcer, (3) the decrease in the quantity of nocturnal gastric secretion, (4) the decrease in the concentration of hydrochloric acid, and (5) a decrease in the motility of the empty stomach as demonstrated by the balloon technic in which contraction is recorded by utilization of the manometer and kymograph.

I have thought it best to attack the problem from the standpoint of a study of the anatomic

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distribution of the vagi nerves in 100 cases in which necropsy was carried out (death being due to causes other than those related to ulcer). I have also attempted to repeat studies of gastric secretion (as regards quantity and concentration of hydrochloric acid) and gastro-intestinal motility among patients for whom gastric neurectomy, either associated with gastro-enterostomy or gastric resection, or performed alone, has been performed. I shall confine the discussion to my own experiences in 21 of these cases.*

First of all, I have preferred to do the procedure through a transabdominal upper left rectus incision, so that I might visualize the ulcer and determine whether or not excision of it is indicated, because of suspicion that it might be either an ulcerating carcinoma of the stomach or a duodenal ulcer with impending obstruction. Therefore, in dealing with ulcerating gastric lesions, I have believed that gastric ulcer should be removed not alone for purposes of biopsy, but also because, since an incision must be made anyway, there is no reason why the entire lesion should not be removed as advocated by Balfour years ago.

If the ulcer were duodenal and it appeared as if obstruction might occur as a result of decrease in the tonicity of the stomach, then I have combined gastro-enterostomy or gastric resection with resection of the vagi nerves (gastric neurectomy). In 7 cases, resection of this nerve has been carried out without performance of any other procedure, and it is only in this latter group of cases, I believe, that the results of the operation can be evaluated, since both partial gastrectomy and gastro-enterostomy will produce a decrease in nocturnal gastric secretion, in gastrospasm and in the concentration of gastric acids. All these are, of course, results also attributed to vagotomy.

I should like to call attention to two very important points in the performance of complete division of the vagi nerves and all their branches at the level of the lower part of the



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esophagus, and in the determination, after the operation, that complete division actually has been achieved.

IN THE first instance, anatomic dissections by my colleagues, Drs. Bradley, Small, and Wilson, have shown that in about 8 per cent of cases the vagi nerves divide into multiple branches around the esophagus just above the diaphragm, and that these branches extend through the diaphragm and terminate in this way in the stomach. It would be very difficult, regardless of whether the surgical approach was made through the thorax or through the abdomen, for the surgeon to be absolutely certain that all the branches had been divided.

Second, the insulin test as described by Hollander for determination of this point must be used with the utmost caution, because the individual response to the quantity of insulin required is variable and is dependent on many factors, which space does not permit me to

*Additional operations have been performed in similar cases by my colleagues at the Mayo Clinic.

enumerate here. Suffice it to say that whenever this test is used, it must be regarded as being accompanied by the possible risk of production of hypoglycemic convulsion in some patients when the blood sugar decreases to that value which is necessary for determination of the function of the vagi nerves in respect to gastric secretion. Hence, when this test is employed, the surgeon must have a physician standing by with a syringe containing glucose and saline solution which can be injected intravenously at the slightest indication of the need for increase in the patient's blood sugar. The test itself consists of injection of 10 to 30 units of insulin in order to reduce the patient's blood sugar to 30 mg. per 100 cc. of blood. If branches of the vagi nerves are intact, an increase in the gastric secretion is regularly found forty to fifty minutes after injection of the insulin.

Indications for resection of the vagi nerves (gastric neurectomy)—At the Mayo Clinic we have decided to employ the procedure for patients who have recurrent ulcers after partial gastrectomy, and in some cases after gastro-enterostomy, for patients who have intractable pain caused by small gastric ulcers which have not healed under a medical regime but which have been proved to be benign, and for certain patients who have intractable pain caused by duodenal ulcers whose response to medical regime has been unsatisfactory and for whom, for one reason or another, partial gastrectomy or gastro-enterostomy does not seem to be indicated. Patients who have nonobstructive duodenal ulcer usually are young, vigorous men who have hyperactive nervous systems.

I have had 3 patients in whom paroxysmal gastro-intestinal atony developed after the operation. In 2 of these 3 patients the condition was associated with gastro-enterostomy. In one it was associated with gastric resection. Two of the 3 patients have responded to the injection of prostigmine. In a third, clinical symptoms and roentgenologic evidence indicated intestinal obstruction, but this was not found at operation; rather the entire small intestine was seen to be dilated with fluid and gas or air.

There was 500 cc. of sterile straw-colored fluid within the abdomen. The patient recovered gastro-intestinal tonicity, and recovery undoubtedly was assisted by the use of an indwelling duodenal tube in which constant suction was maintained.

If the surgeon is to use the procedure of resection of the vagi nerves, I believe it important that he have a thorough understanding of the distribution of the branches of these nerves around the lower end of the esophagus, so that he may carry out a complete procedure surgically. I have described the indications which we at present are using in the selection of patients for the operative procedure at the Mayo Clinic, but it is still too early for me to comment on the results of the operation in comparison with results of such procedures as partial gastrectomy and gastro-enterostomy—for these operations have been used in many cases everywhere for twenty to forty years, and the results are well known.

SURGICAL APPROACH TO CARCINOMA OF THE UPPER PORTION OF THE STOMACH

SINCE Phemister and Allen first reported on the transthoracic, transdiaphragmatic removal of lesions of the upper part of the stomach and the performance of gastro-esophageal anastomosis, 50 patients with such lesions have been operated on in such a manner at the Mayo Clinic. The method lends itself to the removal of lesions which were previously thought to be irremovable except by transabdominal total gastrectomy.

In the decision as to whether such lesions are removable I prefer, first, to make a small upper left rectus incision through the abdominal wall. This permits surgical exploration of the lesion itself and of the liver and pelvis to determine whether the lesion is operable in that it has not invaded adjacent structures, or whether hepatic metastasis or pelvic implants which would make the lesion inoperable are present. This can quickly be determined and is of much less risk to the patient than it would be if the lesion were approached primarily

through the thorax and diaphragm, only to find that it was inoperable. Moreover, the preliminary procedure I have described permits performance of the operation of total gastrectomy in which, in addition to the stomach, the avenues of lymphatic extension in the gastrocolic and gastrohepatic omentum can be excised. Experience and time, I believe, will show that prolongation of life of the patient is greater after such an operation than it is after gastroesophageal anastomosis has been carried out, for after the latter procedure, the avenues of lymphatic extension in the wall of the remaining portion of the stomach and the lymphatics in the attached gastrocolic and gastrohepatic omentum may contain malignant cells. If so, recurrence will ensue.

GASTRIC DIVERTICULECTOMY

Gastric diverticula are rather uncommon lesions of the stomach. Because of that fact and because it has been thought that gastric diverticula produce as few symptoms as do duodenal diverticula, too little attention has been paid to these gastric lesions as possible causes of a type of dyspepsia which actually has some rather characteristic features. Gastric diverticula are located on the posterior wall of the stomach off the lesser curvature, close to the esophageal cardiac orifice. They are false diverticula in which one of the layers of the gastric wall is absent. The neck of a gastric diverticulum is small, approximately a half inch in diameter. An undistended diverticulum usually is approximately 2 to 2½ inches in diameter. Generally, the wall of a gastric diverticulum contains blood vessels; when food is retained within the diverticulum, inflammation then results and gastric bleeding of the oozing type may occur and produce marked secondary anemia.

In addition to the sign of anemia when bleeding occurs from these diverticula, there are such symptoms as a sensation of distressing fullness and pain in the epigastrium immediately after a patient has eaten. In some cases, when superficial ulceration of the gastric

mucosa has occurred, ulcer-like symptoms have been present. At roentgenologic examination, performed elsewhere, of 2 of my patients, the report of "gastric ulcer" had been made. In the 6 cases in which I have operated and which I have reported in detail elsewhere, symptoms disappeared after removal of the diverticulum.

The best approach to these lesions surgically is through an upper left rectus incision. I prefer to use spinal anesthesia because it insures decrease in excursions of the diaphragm and the absence of intra-abdominal movements on the patient's respiration. The blood vessels in the gastrosplenic ligament at the fundus ventriculi are divided and ligated, the fundus is turned mesially, and then the diverticulum can be found in the location previously described. In one case—the second gastric diverticulectomy which I did—I was unable to find the diverticulum at the first operation, but found it and removed it at the second operation which was carried out some months later because of the persistence of the troublesome symptoms that I have described. After removal of the diverticulum, the symptoms completely disappeared.

ASEPTIC VERSUS OPEN GASTRO-INTESTINAL ANASTOMOSIS

ALTHOUGH many types of aseptic anastomosis have been described in the performance of operations on the colon, only recently has interest been stimulated in the use of aseptic or closed anastomosis in the treatment of lesions of the stomach and duodenum. Such an anastomosis is made over clamps, which are then removed and the lumen established forcibly by approximation of the surgeon's fingers through the anastomosis. The operative technic looks better than that employed in the establishment of open anastomosis, but to my mind, the risk of bleeding from the inverted blood vessels in the submucosa of the stomach does not warrant the risk of such a procedure.

I think I can demonstrate that establishment of open anastomosis, with proper attention to surgical toilet and with irrigation of the upper

part of the abdomen and removal of accumulated blood clot, is followed by a minimal reaction. That is, I have studied the temperature charts pertaining to patients on my service who had undergone gastric operations and who were in the hospital in the middle part of July, 1946. These patients do not constitute isolated instances but were all patients who had undergone gastric operations on my service and who were in the hospital recovering from their operation on this particular day. Examination of these charts shows that, as reflected by temperature and pulse rates, there has been a minimal reaction in almost every case except one; in this one case pulmonary atelectasis developed, which, nevertheless, responded well to the usual methods of treatment. At the same time that these patients were in the hospital, there was another patient for whom I had performed ileocolostomy as the first stage of hemicolectomy on the right for an adenocarcinoma of the ileum penetrating the abdominal wall. Open anastomosis also was established in this case. An elevation in temperature of only one degree followed this operation.

It has been my experience, in the performance of open anastomosis, that even when three rows of sutures are used in the anastomosis, bleeding frequently will be seen at the posterior aspect of the anastomosis when the Doyen clamp is released. I always release this clamp before starting the first row of sutures in the anterior portion of the anastomosis and bleeding blood vessels are then ligated with a mattress suture. Blood does accumulate, however, despite this precaution.

I believe the use of warm sterile water to irrigate the upper part of the abdomen after establishment of this type of anastomosis is of tremendous value, and I should like to emphasize particularly the necessity of removal, from under the left portion of the diaphragm, of blood which accumulates during the course of operations on the stomach. In many cases, I have instilled 5 gm. of sulfanilamide in this area and under the liver, but I am convinced

that the most important precautions in the reduction of postoperative reactions caused by disturbances within the abdomen are to be sure, first, that the operative field is completely avascular; second, that blood which has accumulated during the course of the operation is removed; and third, that the patient's stomach and upper part of the intestinal tract are kept empty the first three days postoperatively by means of an indwelling nasal gastric suction tube.

USE OF VITALLIUM, RUBBER TUBES, OR CATHETERS IN ANASTOMOSIS FOR STRICTURE OF THE COMMON BILE DUCT

IT NEVER has been definitely proved that it is necessary to place a foreign-body tube of any type in the anastomosis established between the biliary and intestinal tracts to maintain patency of the anastomosis *if* a sufficient part of the common or hepatic duct is present, without inflammation in its wall, to enable the surgeon accurately to anastomose the duct to the duodenum or the jejunum. When such accurate anastomosis cannot be established, a tube must be used to provide a temporary channel for the transmission of bile and as a splint around which adjacent structures may attach themselves, to assist in the formation of an internal fistula, and to act as an uncollapsible cylinder, the lumen of which remains open unless it is obstructed by bile pigment and other debris.* Such obstruction usually occurs when a rubber tube is used and remains in place for any period, as all of you know who have removed, from a common bile duct, a T-tube which has been in place for more than a few weeks.

The necessity for maintenance of an open lumen in the tube led to Pearse's introduction of a Vitallium tube on the assumption that bile pigments would not be deposited within the lumen of the tube and obstruct it. In the first year or two that Vitallium tubes were used for

*Experience has shown that, with the passage of tubes used without accurate anastomosis between the end of the duct and the intestine, contraction of the sinus occurs, with recurrence of symptoms of obstruction.

this purpose, excellent reports were made of their value on the basis of studies over a short period after the operation. Recently, however, reports have accumulated which indicate that bile pigment does accumulate within the lumina of Vitallium tubes, and that the rigidity of the tube is not without danger in the production of pressure necrosis.

Some of the best results I have obtained in anastomosis of the common bile duct to the duodenum for the treatment of stricture have been achieved without the use of any tube in the anastomosis, but such success is possible only if an accurate anastomosis is established. When I have had to use tubes in anastomosis of the common bile duct to the duodenum, I have preferred to use the Mayo-Sullivan tube, which is a portion of a catheter about which two collars of oversize tubes are fastened. These rubber collars help to maintain the tube in place for about one week to two weeks, unless it is fastened to the duct by a nonabsorbable suture. Even when it is thus sutured, I cannot remember ever having had to remove such a tube secondarily, because all of them apparently have passed from the anastomosis through the intestinal tract.

When the stricture is small and confined to the mid-portion of the common bile duct, so that it can be excised and the ends of the duct approximated, one must not leave within the duct any sort of tube which does not have a chance to pass out of it through the sphincter of Oddi. Such an action can be assured only if a portion of the tube extends through the sphincter into the duodenum and, in such a case, the use of a catheter as recommended by McArthur in 1923 has served a very useful purpose, in my experience. To prevent natural intestinal peristalsis from pulling the tube out of the common bile duct, the tube can be maintained in position by the passing of a heavy silk suture through it, which suture is brought out through the incision and attached to the abdominal wall by tying it over a button. When it is desirable that the tube be allowed to pass out through the intestine (usually within two

to three months), the suture can be removed by pulling on one of its ends.

ANASTOMOSIS TO DUODENUM OR JEJUNUM FOR STRICTURE OF THE COMMON BILE OR HEPATIC DUCT

IN DISCUSSING stricture of the common bile duct, it gives me opportunity to consider the relative merits of anastomosis of the common bile or hepatic duct to the duodenum or jejunum. It has been stated by some that anastomosis to the jejunum is the preferable procedure. When this is done, the jejunum is divided, the common bile duct is anastomosed to the distal portion of jejunum, and the proximal end of jejunum is sutured to the side of the distal portion of jejunum, as is done in the Roux type of gastro-enterostomy. This procedure is based on the opinion that, since air can be demonstrated as being present within the intrahepatic ducts after the common bile duct has been anastomosed to the duodenum, and that since barium administered by mouth can be demonstrated as entering these ducts, reflux of gas or liquids into these ducts is responsible for the episodes of fever, jaundice, and pain which occur in some cases subsequent to performance of biliary-intestinal anastomosis in the treatment of stricture.

In my opinion, however, these symptoms actually are those of obstruction at the site of anastomosis; I believe that they arise because of this obstruction, and that cholangitis is secondary to this obstruction. I think that such symptoms will be found to occur also among those patients who have undergone the Roux type of biliary-jejunal anastomosis, if obstruction occurs at the site of anastomosis. Moreover, the presence of air likewise can be demonstrated within the hepatic ducts after performance of biliary-jejunal anastomosis. In other words, in my opinion, the disturbance of hepatic function characterized clinically in most cases by pain, and in others by fever or jaundice, subsequent to performance of biliary-intestinal anastomosis, is the result of stasis within the biliary tract secondary to incomplete

obstruction at the site of anastomosis, and is not the result of reflux of gas or liquids up into the common bile and hepatic ducts.

I think this point is worthy of emphasis, because for the very seriously sick, jaundiced patient who has disturbance of hepatic and renal function associated with stricture of the common bile duct, the simplest and safest type of operation which will relieve the obstruction is anastomosis of the cut ends of the duct, if the stricture can be excised. If the stricture is too extensive or involves the lower end of the duct, the alternative is anastomosis of the duct above the stricture to the duodenum. When I recently mentioned this point to a visiting French surgeon, Dr. Robert Soupault, he said that he had studied the same problems experimentally in dogs, and was able to demonstrate specifically that cholangitis was not produced by the reflux of gas or fluid up the common bile duct and hepatic duct, where the effect of the sphincter of Oddi was lacking as in a biliary-duodenal anastomosis, but that it was produced by obstruction at the site of anastomosis.

NEOPLASMS OF THE ISLANDS OF LANGERHANS

I SHOULD like to close this consideration of some of the advances in the treatment of lesions of the upper part of the abdomen by referring to some of the problems associated with hyperfunctioning adenomas of the islands of Langerhans of the pancreas. These adenomas produce paroxysmal hypoglycemia. I am sure that all physicians are acquainted with the clinical syndrome which appears as a result of hyperinsulinism. The patient's blood sugar decreases to lower than 40 mg. per 100 cc. of blood. The patient becomes drowsy and frequently may lose consciousness. Some patients in whom this has occurred actually have been arrested by the police because of suspected alcoholic or drug intoxication. Frequently, neurologic symptoms have developed during the hypoglycemic episodes and in some cases, the patients have become so unusual in their

reactions that they have been judged to be insane.

Space does not permit a discussion of the detailed metabolic studies necessary to exclude other causes for the paroxysmal hypoglycemia. I should, however, like to refer to the position of the hyperfunctioning adenomas in the pancreas and some of the difficulties which I have encountered in determining the presence of these tumors. Since they vary from a few millimeters to more than 2 cm. in diameter, it can be readily understood how the smaller tumors might escape detection, especially those located in the substance of the gland.

I have found that the best approach to the pancreas is through the gastrocolic omentum; the stomach is reflected upward and the pancreas is exposed for visual inspection and manual palpation. The sites at which the tumor most frequently is likely to be overlooked are the head and tail of the pancreas and the undersurface of the pancreas. If the pancreas is picked up between the surgeon's thumb and finger in such a way that he can palpate it anteriorly and posteriorly, even small adenomas can be palpated.

The small tumors in the substance of the pancreas, and especially those in the head of the pancreas, often may escape detection if any means other than removal and serial section of the pancreas is employed. It is our custom, therefore, when an adenoma is not palpated, to do subtotal pancreatectomy in which all but the head of the pancreas is removed. Removal of the spleen and splenic vessels facilitates this procedure. It can be readily seen that if all of the pancreas except the head is removed, there is probably an 80 per cent chance that any tumor of the pancreas that had been present also is removed, since in about 20 per cent of cases the adenoma is located in the head. If, after this procedure, the patient continues to have symptoms, the head of the pancreas should be removed.

As is true when hyperfunctioning tumors of the ductless glands are removed, an overcompensation in the opposite direction occurs, and must be compensated for. For example, when

a hyperfunctioning adenoma of the islands of Langerhans producing hyperinsulinism occurs, removal of it produces temporary hypo-insulinism with high values for blood sugar which may require the administration of insulin for correction.

SUMMARY

The significance of anatomic dissections of the vagi nerves of 100 human beings and a study of resection of the vagi nerves in the treatment of peptic ulcer have been considered. The present indications for the use of this procedure have been enumerated.

Transabdominal exploration of lesions of the upper half or two-thirds of the stomach would seem to be preferable to transthoracic and transdiaphragmatic exploration. Gastric diverticula, although rare, produce a characteristic group of symptoms which are relieved by the removal of the diverticula. The open type of gastro-intestinal anastomosis is preferable to the closed, so-called aseptic method, for it al-

lows complete hemostasis and is followed by a minimal post-operative reaction, especially when the upper part of the abdomen is irrigated with water, and blood is removed from under the left side of the diaphragm. No tubes of any sort are required if an accurate anastomosis can be made of the common bile duct above the site of stricture to an opening in the duodenum. The use of a piece of rubber tube or a catheter as a temporary "scaffolding" in such an anastomosis is preferred to the use of a vitallium tube. If that portion of the common bile duct affected by stricture cannot be excised and the ends of the duct approximated, anastomosis of the common or hepatic duct to the duodenum is preferred to anastomosis of these ducts to the jejunum. Although most hyperfunctioning adenomas of the island of Langerhans are palpable, some are not. Whenever one thinks that such lesions may be present, but they cannot be palpated, then subtotal pancreatectomy is advisable in the hope that the adenoma will be found in the substance of the removed portion of pancreas.

MILIARY TUBERCULOSIS

Miliary tuberculosis and tuberculous meningitis are two of the most fulminating and fatal forms of tuberculosis. Because of that fact, investigators at the Mayo Clinic selected 5 such cases upon which they could study the action of streptomycin. Although all the patients died, the effect of the antibiotic on the progress of the disease was evident.

Streptomycin caused a regression and healing of the miliary tubercles in the lung, choroid layer of the eye, liver, and spleen. Tuberculous meningitis was inhibited in its development in one patient and prevented or cured in two others. Except for renal tubular damage in one patient, no toxic effects were observed. Because of the gravity of the prognosis in these types of tuberculosis, the results are regarded as distinctly encouraging.

The Operative Treatment of Aneurysms and Arteriovenous Fistulas

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ACCOUNTS of injuries to blood vessels in warfare have been recorded since the beginning of history, and the attention of surgeons has of necessity been primarily directed toward their treatment because of their often fatal nature.

The number of such injuries has increased steadily, probably because of the introduction of higher velocity projectiles of smaller caliber. The fragments of these exploding missiles may produce as many as two hundred small individual wounds scattered over the body without causing death and thus increasing the chance of trauma to blood vessels.

This report is concerned with the operative treatment of traumatic aneurysms and arteriovenous fistulas, approximately 500 of which were treated at the vascular surgery center of an Army general hospital over a period of three years.

If a vessel is only partially severed, the wound tends to enlarge in the long axis of the vessel owing to retraction, and hemorrhage is apt to

be profuse. If the wound in the soft tissues overlying the vessel is large, hemorrhage, of course, would be external and probably would require medical control. But if the wound is small, the overlapping of the various muscle, fascial, and skin planes may prevent the escape of blood externally. This results in a hematoma which may become a false aneurysm.

However, in instances with a small external wound, when the vein is injured at the same time, an arteriovenous fistula may result, the artery and vein communicating directly or through the medium of a false sac. In either case it is well to remember that some blood continues to flow through the distal portion of the artery, thus nourishing the part beyond, and that collaterals develop rapidly. Therefore, immediate operation is always contraindicated unless necessitated by hemorrhage or rapid enlargement of an aneurysmal sac which compresses the vessels of this collateral circulation.

Openings in blood vessels produced by small missiles may for a time produce no symptoms. For this reason, these lesions are frequently overlooked, particularly if more striking or extensive injuries are present. Aneurysms of various types will be overlooked unless every wound is carefully examined, particularly by auscultation.

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The differentiation of a false arterial aneurysm from an arteriovenous fistula is extremely important, since the sequelae, the general and local effects, as well as the treatment of the two conditions, vary greatly. The differential diagnosis is not always easy, but as a rule the arteriovenous communication is characterized by continuous vibratory thrill and a loud, rough, continuous murmur with systolic intensification, whereas in the false aneurysm there is distinct pause between the systolic and diastolic phases, and more often the murmur is heard only in systole.

In the 500 instances of aneurysms and fistulas, approximately 100 were the false traumatic arterial type and the remainder were arteriovenous fistulas. Since anatomically they presented many of the same problems, they will be discussed together. They were encountered in practically every named blood vessel in the body, with the exception of the aorta, and many presented varied problems of approach and treatment.

In the case of a partial division of an artery resulting in a false aneurysm, the treatment followed was generally according to the Matas' principle of opening the sac under a tourniquet if possible, locating the openings within the sac and suturing within the sac. Where nerve injuries were present and a neurolysis or nerve suture had to be done at the same time, this method could not be used.

The principal method of treatment of arteriovenous fistulas was quadruple ligation and complete excision of the lesion. Although it is recognized that repair of the artery by one means or another is preferable, it usually cannot be done because of scar tissue.

I SHOULD like to stress the fact that proximal ligation of the artery should not be done as a means of treatment as gangrene is apt to follow, the fistula is not cured but is still being fed through collaterals, and what blood might go through the distal artery is cut off. Likewise, proximal ligation of artery and vein will not

cure the condition—since the fistula is still present—nor will ligation of all the main vessels cure it if there are any communicating vessels or collaterals left. Therefore, complete excision is certainly the method of choice, and the circulation, if time is allowed for these collaterals to develop, will usually be improved.

If complete excision is done, an important technical point must be stressed—the artery proximal to the fistula should first be isolated but not ligated. If it is ligated, it is more difficult to locate the fistula. After location of the proximal artery and its isolation, the distal artery and vein may be ligated and divided; then the proximal artery may be ligated and divided; and finally, as the last step in the procedure, the collateral vessels, with the proximal vein, may be divided. In repairing arteriovenous fistulas this can sometimes be done, usually with sacrifice of the vein, with removal of a portion of the vein and an actual suture of the artery. Or, many times the vein itself may be utilized but sacrificed, and the opening between artery and vein approached transvenously, using the remaining portion of the vein to reinforce the sutures.

Excisions of arteriovenous fistulas, of course, must eventually be done if they are of any size, because of the strain on the heart due to increased cardiac output resulting from the shunting of blood through the fistula.

Not infrequently aneurysms of this kind on the scalp become cirroid with multiple communications, and the following method of treatment is advocated: First, ligation of all main vessels, such as the superficial temporals or even both external carotids, the turning down of a scalp flap, going completely through the galea to the pericranium, the turning back of such a flap and the dissecting out of the communicating vessels by going through the galea from the underneath side. Large arteriovenous fistulas of this type are particularly difficult because of the inability to control bleeding, no tourniquet, of course, being possible.

Twelve instances of arteriovenous fistula have been encountered in the vertebral vessels. They are by far the most difficult to reach in the

neck, since the vertebral artery runs through the foramina and the transverse processes of the upper seven cervical vertebrae. In its lower portion the fistula is best approached through the sternomastoid muscle, displacing the carotid vessel anteriorly and then reaching the vertebral vessels by removing the transverse processes of the atlas and axis. They may have to be removed in order to reach the vessels themselves.

WE HAVE not hesitated at any time to remove the clavicle in order better to expose lesions of the lower carotid vessels or the subclavian or even the axillary in the first portion. If the clavicle is removed subperiosteally there is little danger of injuring underlying structures unless an aneurysm be present which actually has its wall formed by the clavicle. We believe it is unwise to replace removed portions of the clavicle because it is not needed for any particular function and if replaced, painful union is apt to occur.

After removal of a portion of the clavicle, the incision may be extended upward to expose the lower carotid and first portions of the subclavian vessels. Section of part of the sternomastoid muscle exposes the vertebral vessels, thyrocervical trunk, and subclavian vessels. Additional exposure is had by cutting the tendon of the anterior scalene muscle which overlies the subclavian artery.

The iliacs, internal, common, and external, are best approached through a retroperitoneal incision, much as one would approach surgically the lower ureter. The gluteal vessels are approached directly through the buttocks, but after preliminary ligation, either complete or temporary, of the common iliac artery through a retroperitoneal incision.

The femoral vessels in the thigh are best approached along the sartorius muscle and, if necessary, preliminary ligations may be made through a transverse incision at or below or just above Poupart's ligament. In the lower femoral and upper popliteal vessels, an incision posterior to the quadriceps is done, but with the

knee flexed and externally rotated. When the deep fascia is opened, the sartorius muscle retracts posteriorly and exposes Hunter's canal in its lowest portion.

It is important, I think, in approaching any blood vessel or making any incision, not to cross skin folds transversely. An S-shaped incision, particularly in the popliteal space, is by far preferable to one which is transverse. The same is, of course, applicable to crossing skin folds either in the neck or in the cubital fossa.

We have done a number of operations in which we felt it was necessary to remove the upper portion of the fibula, including the head, in order to reach the posterior tibial, the anterior tibial, and peroneal vessels. Unless that is done, uncontrollable hemorrhage may be encountered because of retraction of the vessels through the interosseous spaces. We have not felt, and I am sure most orthopedic surgeons will agree, that it is not necessary to replace the upper end of the fibula. There is no instability of the knee following such a procedure. The important point is to isolate the peroneal nerve completely to prevent any possibility of injuring it, and to remove the bone subperiosteally, usually at the head, by sharp dissection. This is done in the lower end by use of a Gigli saw. When this procedure is followed, the upper portions of the posterior and anterior tibial and peroneal vessels are immediately exposed by the muscles.

For incisions lower down, of course, it is not necessary to remove any bone, but the posterior tibial vessels and peroneal vessels are approached through an incision exactly one finger-breadth behind the posterior border of the tibia, through an incision which may be extended a little further up or down as far as the internal malleolus.

For approach to the plantar vessels, incision is made on the inner side of the foot and not on the weight-bearing sole of the foot, since such scars are usually painful. The abductor hallucis is detached and the incision is made following the long tendon into the sole of the foot between the short flexors where the plantar arch is easily exposed.

OPERATIONS which we have performed on the lower extremities were done almost entirely under continuous spinal anesthesia. Operations on other parts of the body were usually done under pentothal sodium supplemented by nitrous oxide and oxygen. There were no complications of consequence attributable to the anesthetic.

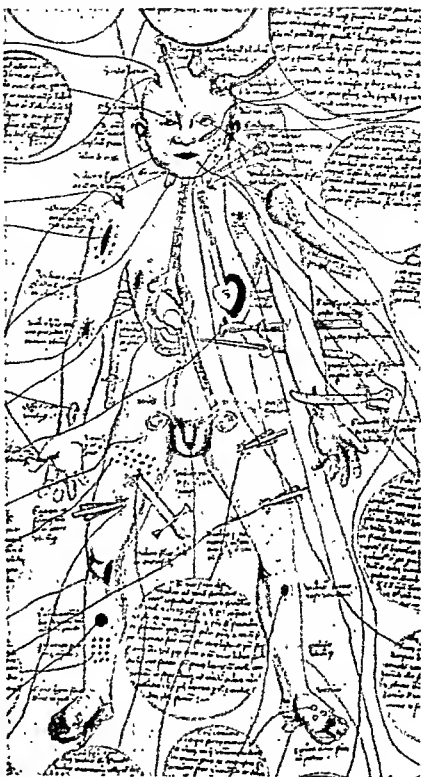
All together, half the operations performed required more than three hours and some as much as seven hours.

There were no instances of gangrene of an extremity in this series. Sympathectomy and sympathetic block were rarely performed either before or after operation, although the advantages of it are thoroughly appreciated.

The time interval between the origin of the wounds and the operation averaged three months, and it was rarely less. Thus, ample time for the development of collaterals was allowed. Had operations of necessity been performed at an earlier date, no doubt sympathetic interruption would have been more frequently performed.

There was but one death in this series and that was due to a secondary hemorrhage following excision of an arteriovenous aneurysm of the subclavian vessels. The fistula was so close to the aorta that the vessels could not be transfixed, a procedure always carried out in operating upon vessels of any size. There were two instances of cerebral anemia with paralysis following operation on the carotid vessels. One of these was transient, the other permanent.

In 10 patients, more than 1 operation was necessary to effect a cure. In 2 of these cases, 4 operations were performed. Three patients were not cured by operation—all of them had arteriovenous fistulas of internal carotid vessels at the base of the skull which could not be completely eradicated because of their position.



The Wound-Man. This mnemonic figure illustrates the various possible injuries to which the human body was supposed to be subject. About A. D. 1500. Reproduced from "The Fasciculus Medicine" of Johannes de Ketham, Alemanus, Facsimile of the First (Venetian) Edition of 1491.

The Diagnosis of Activity in Pulmonary Tuberculosis

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THERE is probably no single word in the vocabulary of clinical tuberculosis more widely employed than the word "activity," and no concept more widely misunderstood than the one indicated by that word. The ancient fallacy still persists that rales arise in moisture, and moisture signifies inflammation and hence, activity. An equally prevalent fallacy, perhaps more dangerous because it pretends to be based on more precise observations, is that activity is generally accompanied by some degree of constitutional disturbance, which, however mild, will be reflected in slight changes in temperature, pulse, weight, appetite, physical energy, etc. I frequently encounter such misconceptions, not only in the minds of medical students but also in those of experienced practitioners and skilled internists.

There has probably never been a period when a clear understanding of the subject of activity in tuberculosis was quite as important as it is today. The introduction of the miniature film technique, and its use by the military services, and in industrial surveys, have made the public

"chest x-ray conscious" to an unprecedented degree. It has been the general experience that two-thirds to three-fourths of all cases of tuberculosis discovered in mass x-ray surveys of apparently healthy groups of our population are neither obviously active nor obviously healed, but belong to that large in-between group which requires study and observation to determine the presence or absence of activity.

First, what do we mean by activity? The word obviously implies a disease process which is undergoing a change in its status as opposed to one which is stationary. But this definition is neither accurate nor sufficiently comprehensive. A change in status may be, in some cases, merely a histological change, having no immediate clinical significance. For example, it is entirely possible to have very gradual caseation going on in the center of a well-encapsulated focus, either in a lymph node or in the lung parenchyma, over a period of years during which the subject remains in good health. We must, therefore, recognize the possibility of *pathological* activity, or change, without *clinical* activity.

Changes may also occur in either of two directions, the progressive or the retrogressive. Retrogressive change may or may not have clinical significance, depending upon whether the observed retrogression occurs near the beginning or near the end of the healing process.

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Furthermore, we often encounter cases in which the disease, though not healed, remains stationary for varying periods of time before resuming its progression. Therefore, if we wish a concept of clinical activity which is synonymous with need for treatment it must include three distinct groups of cases—first, those showing anatomic progression; second, those which are anatomically stationary but not healed; and third, those which are retrogressive but not yet safely healed.

As aids in determining whether or not a case requires treatment, the symptoms, physical signs, laboratory data, and x-ray picture may all be used—or misused. The symptoms of pulmonary tuberculosis are familiar to all of you. For convenience they are often divided into two groups: the local symptoms, consisting of cough, expectoration, hemoptysis, and pleuritic pain; and the constitutional symptoms, consisting of fever, tachycardia, night sweats, dyspepsia, loss of weight, and loss of strength. The late Dr. Lawrason Brown long ago pointed out that generally speaking the local symptoms were more useful in establishing the *presence* of the disease, while the constitutional symptoms were more significant as indicators of *activity*. No one of the symptoms is peculiar to tuberculosis. When only one or two of them are present they may often be due to some other cause, and erroneously attributed to the minimal lesion shown in the x-ray film. The only safeguard against this error, if one has not had sufficient experience in evaluating the symptoms, is to rely upon serial x-ray films as the best guide. When a number of the familiar symptoms are present, and particularly the constitutional symptoms, the activity of the disease is usually so obvious that it is not a problem.

The more common and by far the more serious error, however, is to exclude activity because of the absence of all symptoms. It cannot be emphasized too strongly that tuberculosis, both in its onset, and during the early period of a relapse, is characteristically a symptom-



RAYMOND C. McKAY

free disease. We dare not depend upon symptoms, or await the development of symptoms, to confirm the presence of activity. To do so is to lose the most favorable moment for treatment. Two national surveys have shown that when the diagnosis is based upon symptoms, 87 per cent of the cases will have developed advanced disease. With few exceptions the beginning of symptoms indicates a stage of acute progression occurring several months after the actual onset of activity. It has been a very discouraging experience to see an increasing number of our hospital beds filled with patients whose symptom-free, early disease was discovered in an industrial survey or an army induction examination a year or so earlier, but who refused treatment and continued to work until they felt sick and had advanced disease. Our public requires a large dose of education in this matter; let us hope that most of it will be forthcoming from physicians rather than be left to lay organizations and life insurance companies.

PHYSICAL signs are of still less value than symptoms in the determination of activity. Inspection, palpation, and percussion are entirely worthless, and auscultation is not much better. Coarse, or moderately coarse, moist rales, when present, do usually indicate activity, but they are rarely present in cases in which activity is a problem, and they are often absent, even in far-advanced disease. Conversely, rales of the fine, or moderately coarse, dry type are often present throughout the entire life of a person with well-healed tuberculosis.

Like symptoms and physical signs, the laboratory helps us out occasionally by confirming a suspicion of activity, but is undependable for the purpose of excluding it. The finding of tubercle bacilli in the sputum, or in the gastric contents of patients who have no sputum, is always an indication for treatment, and the search should never be neglected in questionable cases. The sedimentation rate is usually elevated in frankly active cases in which its help is not needed, but its failure to reflect lesser degrees of activity and its frequent elevation from other causes make it of very limited value in pulmonary tuberculosis.

A great amount of work has been done in correlating the differential cell count of the blood with the type of pathological reaction which prevails in the tuberculous process; it is well established that a close correlation exists. Those who have done research on the subject are naturally enthusiastic about it, and they continue to urge blood studies as a guide both to activity and to prognosis. Blood studies, however, are of little use to the doctor in practice. They require skilled technical assistance, and a degree of expertness in interpretation which is not generally available. Even more serious limitations are that the changes are not specific for tuberculosis, and thus far it has not been shown that they precede the anatomic changes. For these reasons the consensus among clinicians is that the x-ray picture still remains a more accurate, sensitive, and dependable barometer of intrapulmonic weather than is the blood picture.

The very great superiority of the x-ray film

over all other guides to activity in pulmonary tuberculosis makes it all the more important that we recognize its limitations, which, fortunately, are minor, and learn to use it to the greatest advantage. It requires comparatively little experience for anyone to learn to recognize, on the one hand, the extreme type of so-called "soft" shadows, with indistinct borders, which signify the active, exudative, pathological reaction, and, on the other hand, the so-called "hard" shadows, partly or largely linear in configuration, and with sharply defined borders, which signify a well-healed fibrotic reaction. In between these two extremes is a large group of cases in which the most experienced and expert interpreter will be unable to differentiate active from inactive disease by a single film. In these cases there is no substitute for the careful and detailed comparison of serial films made at intervals of one to three months. In making such comparisons it is important to keep in mind the following points.

If one of the comparison films has received a heavier, and the other a lighter, exposure, the latter will give the illusion of a general increase of the disease. This can be checked by comparing the shadows cast by the normal structures. Then one should look for any localized changes, which are greater in degree than those generalized changes shown in both the normal and diseased areas.

Accurate comparison also requires that the lungs be inflated to the same degree in the two films. Poorly inflated lungs, even if normal, will appear to be diseased in comparison with better inflated ones, and any disease in them will cast exaggerated shadows. The depth of inspiration is easily checked by counting the posterior ribs down to the dome of the diaphragm. The mechanical effect of under-inflation is even more deceptive when it occurs on one side only. This is often caused by such things as pleural thickening, even when of slight degree, by a quantity of air or fluid in the pleural cavity, by paralysis of one diaphragm, or by displacement of the mediastinum from any cause.

Another factor which very often causes difficulty is slight rotation of the patient, either



Figure 1



Figure 2



Figure 3

to the right or to the left. This obviously presents the disease structure in a different sectional plane and may alter its contour. The presence and degree of rotation are easily checked by comparing the position of the medial ends of the clavicles with relation to the spine.

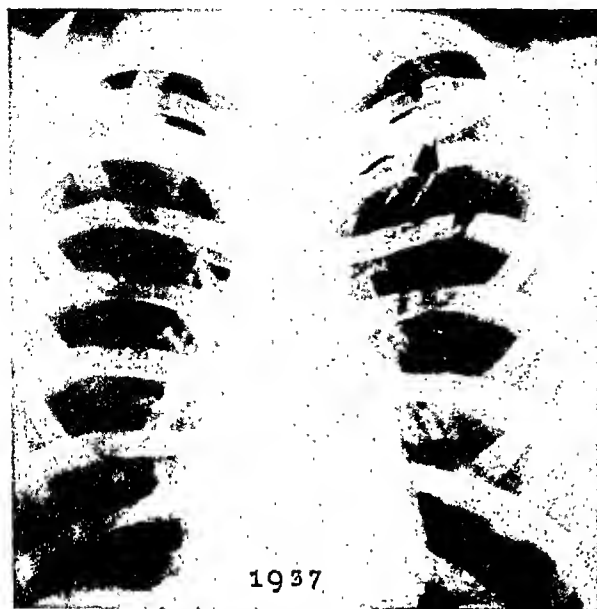
Perhaps the most common source of error in comparing films is failure of the interpreter to take account of the differences in the angle at which the rays coming from the tube impinge upon the chest. This is rarely, if ever, sufficient in degree to make significant changes in the contour of the shadows, but it very often changes the position of disease shadows with relation to the rib shadows. In exceptional cases the entire shadow of an early, active focus of tuberculosis can, in one film, be concealed behind a rib, and in another be clearly silhouetted against an interspace. This explains the familiar observation that at least half of the value of stereoscopic films comes not from viewing them stereoscopically, but from the comparison of two images made at different projection angles. In this respect the clavicle is of even greater importance than the ribs, since its position with relation to any portion of adjacent lung can be

changed not only by the projection angle, but by the position of the patient's highly mobile shoulders. Thus, a slight change in the position of the clavicle will often give the illusion of progressive disease by revealing more fully shadows which were partially concealed, or vice versa.

To illustrate these points the following cases, and the accompanying films, are presented.

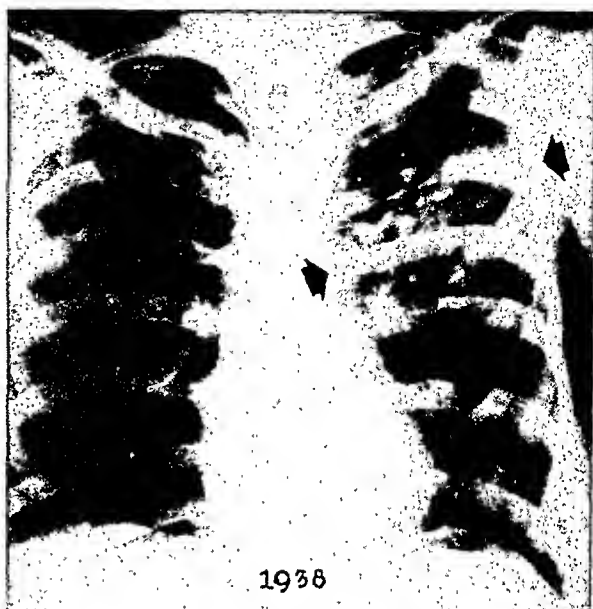
Case one—In Figure 1 it is easy to see the disease in the top of the right lung field above and below the clavicle. This nurse had an acute sinusitis, and because of a little cough, an x-ray examination was made, and this disease was discovered. We were uncertain about the activity, but the shadows showed none of the very hard or linear characteristics of healed disease; on the other hand, they were well defined and did not have the fuzzy borders which characterize acute disease.

Serial films were made, first at intervals of two to three months, and later once or twice a year for a period of six years, during which time she remained in continuous good health. Then she developed this obvious relapse with a little fresh disease and a small pleural effusion at the base (Figure 2). A year of bed rest fol-



1937

Figure 4



1938

Figure 5

lowed, at the end of which there was not only resolution of the increased disease, but there was also resolution of much of the original disease as is shown in Figure 3.

This case illustrates one phase of the problem of activity which is very important and which is probably the least well understood, namely, the capacity of tuberculosis to remain for an indefinite period of time entirely unhealed but not progressive, in what might be described as a state of suspended animation. For such a condition to persist as long as in this case—six years—is unusual, but periods of from several months up to one or two years are fairly common.

Although no particular harm resulted to this girl from the delay in treatment, one could have anticipated the final event by asking oneself at the outset not whether these were the shadows of active disease, but whether they were the shadows of healed disease. By reversing the question in that way I think it is more easily answered from the original film.

Case two—Figure 4 shows very slight tuberculosis under the first rib, dipping down into the interspace. If you have any difficulty in seeing it, compare the opposite interspace and

note that it is definitely clearer. We had previous films showing the absence of these shadows, and for that reason only we knew that it represented active disease.

Treatment was advised, but the girl was absolutely symptom-free and felt herself to be perfectly well; she refused advice and went her way. One year later a film showed the widespread, far-advanced bilateral disease that is revealed in Figure 5.

I have seen this same sort of experience very many times in men whose disease was discovered in industrial surveys and in induction center examinations, and who refused treatment until it was too late, because they felt perfectly well and were not disposed to alter their way of life because of some mere x-ray shadows.

Case three—This represents the more chronic type of case in which the determination of activity may be still more difficult. This patient also had no symptoms. This was a pre-employment examination in an industrial plant. The film showed the character of the shadows in both apices to be rather typically hard, representing a predominantly fibrotic reaction. We, at first, were at a loss to know for certain



Figure 6



Figure 7



Figure 8

whether or not the fibrosis was covering up some smouldering activity. In this case the laboratory helped out, and repeated sputum examinations finally revealed tubercle bacilli. In similar problems sputum examination often provides the quickest solution, but if it remains negative one must depend upon serial films.

Case four—Figure 6 shows obvious slight mottling in the first interspace as indicated. The patient was given about five months of bed rest. In Figure 7 it can be seen that the shadows have largely but not completely disappeared—very gratifying x-ray improvement for that period of time. Since the patient had had no symptoms at any time she was mistakenly allowed to return to work following this film.

Figure 8, taken several months later, reveals a residue of the original disease and also the relapse. In this case, the early x-ray improvement was misleading. Experience has shown that such early active lesions treated by rest usually require at least a full year of rest, no matter how conspicuous the x-ray clearing of the shadows may be during the first few months.

Case five—This patient had had a typical cigarette cough for a number of years and recently she noticed that the character of her

cough had become a little different, and a small amount of thicker sputum than she had ever raised before made its appearance. Her alert doctor promptly ordered a film which showed every appearance of well-healed disease, but the sputum examination showed bacilli. The problem was to reconcile the shadows of apparently healed disease with the presence of tubercle bacilli. Stereoscopic films in two good hospitals failed to show any evidence of cavity, and the source of the positive sputum remained a mystery, although several good roentgenologists and a number of experienced clinicians viewed those films.

In cases like this, resort to some one of the special x-ray views is often of great help. There is a variety of such special views—obliques, laterals, the heavy penetration made with the Bucky-Potter diaphragm, stereoscopic films, laminagrams, and so on. One which is perhaps least often used and which we have found valuable in tuberculosis is the so-called lordotic view in which the patient is made to lean sharply backward. This gets the clavicles completely out of the way and widens the interspaces in the upper part of the chest. With the lordotic view in this case, a 2-cm. cavity in this



Figure 9



Figure 10

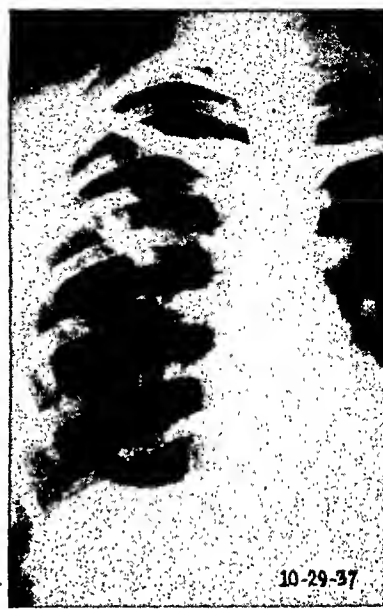


Figure 11

area was clearly outlined, making the source of the positive sputum quite apparent.

Case six—Figure 9 shows a very slight shadow in the area marked. Something over a year later the shadow appeared unchanged as is shown in Figure 10. It is a little farther removed from the rib in this film and its silhouette is more sharply defined. It has all of the superficial appearance of an inactive and healed, or at least partially healed, lesion.

Five months after that last film, another serial film (Figure 11) revealed an acute flare-up of the disease. This was discovered before the patient had any symptoms. She was still in perfect health. Ordinarily one would expect symptoms to make their first appearance soon after the disease process reached this degree, but this case again illustrates the great importance of serial films.

Case seven—The problem of activity in tuberculosis becomes infinitely more difficult when it is complicated by the presence of silicosis. We repeatedly see the well-known conglomerate

shadows of silicosis which, as many of you doubtless know, often represent only old obsolete infection. On the other hand, we often see similar shadows so disposed, extending out to the periphery or with indistinct borders, as to make us suspect that there is latent or smouldering tuberculosis in the background.

In this case films were made several months apart. We thought the second film showed slight but definite progression of the shadows. The silicotic nodulation was also distributed through the lung fields. This patient, an old moulder, was advised at that time, in 1935, that he probably had complicating tuberculosis. However, he felt well and against advice went back to work at his job of moulding.

Ten years later he was admitted to the hospital with advanced tuberculosis with large cavities in both apices. Ten years is an exceptionally long period of time, but over and over again in silicotics we see the warning signs of smouldering tuberculosis which does not develop into frank clinical activity with symptoms for periods of one, two, and three years.

Carcinoma of the Colon

THOMAS E. JONES

THE CLEVELAND CLINIC, CLEVELAND

MALIGNANCIES of the colon still are a tremendous job. The job can be made a little easier for the surgeon if an earlier diagnosis is made.

I want to devote most of this paper to the early diagnosis of carcinoma of the colon and rectum. One thing must be realized: from an anatomical standpoint the surgeon has gone just about as far as he possibly can in the eradication of malignant disease of the colon. The kidneys have been removed with the growth, parts of the stomach have been removed with the transverse colon, the spleen, uterus, and adnexa as well as parts of the bladder have all been removed. We cannot go any further from an anatomical standpoint. Future results are dependent entirely upon early diagnosis; that, of course, rests squarely upon the practitioner, whether he is a surgeon or a medical man. The surgeon knows very well at the time of operation what a tragedy it is when he fits into the picture the history that the patient has had symptoms for six months, nine months, a year, or even longer, without adequate investigation. Those are the sins of omission, of course, and not the sins of commission.

NOTE: Presented before the meeting of the Interstate Post-graduate Medical Association of North America, Cleveland, Ohio, October 15 to 18, 1946.

Frequently we are asked, "What are the symptoms? How can you find out when a person has an early carcinoma of the colon?" Those are very difficult questions to answer. Unfortunately, there is no characteristic syndrome or any group of symptoms whatsoever for carcinoma of the colon. The symptoms vary greatly for the reason that the colon is different anatomically and physiologically in its various segments.

I think the greatest pitfall in diagnosis is, very simply, that the physician ordinarily associates cancer of the colon with obstruction. Probably that goes back to his intern days when he had to get up in the middle of the night to operate upon an acute obstruction, and after the patient died, he found it was cancer of the colon. That lingers long in his memory—that cancer is a growth which obstructs the lumen. Of course that is not entirely true. On the right side of the colon, the cecum, and ascending colon, the lumen is very large anatomically. Embryologically it rises from the midgut. Its function is entirely different from that on the left side. It is where the absorption takes place. The growths are flat and ordinarily there is no obstruction whatsoever because the contents are liquid on the right side of the

colon. Only occasionally do you get some obstruction as a first symptom on the right side, and in those, only where the ileocecal valve is definitely involved. In the right side of the colon that is a very rare condition.

The symptoms of a neoplasm on the right side are those of a physiological nature. The patient will have digestive symptoms, a vague epigastric discomfort, perhaps something like a chronic appendix. The patient loses weight because something has happened to interfere with normal absorption. There is generally a marked anemia with lesions on the right side of the colon, owing to the lack of absorption of various foods. These patients go on being treated for anemia for months and months before the diagnosis is actually made. They are treated with liver, iron, and all sorts of things without improvement, and finally an investigation is made, and the disease is disclosed.

On the left side of the colon the lumen of the bowel is smaller, the muscular coat is thicker, and the stool is firm; therefore we are more apt to get obstructive symptoms earlier than on the right side. Anemia is not so prominent with lesions of the left side unless there is definite metastasis or liver involvement. Trauma will cause some bleeding and mucus from a neoplasm in the left side of the colon.

In the next group, relating to the rectum, diarrhea is a very prominent symptom, and this again throws one off. We have gone through various periods of different treatment for diarrhea in the past twenty years. These patients used to be treated with vaccines and serums for colitis. When that treatment failed to cure even colitis, let alone cancer, we got tired of it. Then another very popular agent came along, the sulfa drugs, and now all these patients I find have been given a course of sulfasuxidine and all the other sulfa drugs for many weeks or months before the real diagnosis is made. This is because the patient has mucus, diarrhea, and blood. But it is a false diarrhea, not a true diarrhea.

I have often said that the pediatrician makes all of his diagnoses of gastro-intestinal com-



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plaints by looking at the stools. If the physician would look at one of these so-called diarrheal stools in adults, he would know very well that it was not a true diarrhea but a false one, the stools being frequent emissions of mucus, pus, and blood.

THE diagnosis of any of these cases must be made in a methodical manner, and unless it is done in a methodical manner, there will be errors. The first and most important procedure is an accurate sequential history. Anybody who comes in complaining of any bowel disturbance whatsoever, whether of diarrhea or constipation, gives a good sequential history of the condition. And the second factor is a thorough abdominal examination.

Third, of course, is a digital examination of the rectum. This should be done routinely in all cases regardless of what the patient has and particularly in cases of suspected malignancy. Care must be taken to make this examination painless. As specialists we find that many peo-

ple have been driven away from other doctors perhaps two or three months before because the examination was so painful that they hated to go back. It is a simple but important matter to see that the finger is well lubricated up to the hilt.

If you find fissures or painful hemorrhoids and you want to do a sigmoidoscopic examination, see that the patient has some sort of anesthetic to make the examination painless. Be sure that you have a well-cleaned bowel. There is no need examining on the day the patient comes to see you. See that the bowel is well prepared on the night before, if he has no obstruction, and do the sigmoidoscopic examination under ideal conditions.

If this fails to give information, the next thing to do is to have an x-ray examination of the colon. Unfortunately in the past it has been either too easy or too cheap to say, "Go on and have an x-ray of the colon and see what is the matter." The trouble with that is that 75 per cent of all malignancies of the colon are in the rectum or lower sigmoid, what we call the rectosigmoid. The x-ray man knows very well that this is a blind spot and that you can have a carcinoma of the rectum as big as an egg and still have a perfectly good-looking x-ray picture. Therefore an x-ray examination is the last thing to order.

In these days many people on the outside are trying to make rules and regulations for us. It might come to that if we do not do a better job than we have done heretofore in early diagnosis. Following a few rules among ourselves may be a good step forward. Suppose an x-ray man had to have a written statement that a digital and proctoscopic examination had been made before he was allowed to do an x-ray of the colon. If we had a simple working agreement like that, much of our trouble today would disappear automatically and many x-rays of the colon would be automatically eliminated. I am sure, however, that the x-ray man would not worry about that because at least there would be one mistake that he might not have made.

Don't use the x-ray man as a laboratory man.

Use him as a consultant. After your preliminary examination and history, you can give him some idea, perhaps, of what you are looking for. If he knows what you are looking for, he can help in the examination to show up various things; furthermore, he will be interested in so doing.

If everything in the examination fails, don't discharge the patient completely; keep him under observation and repeat this performance six to eight weeks later if it is necessary.

MANY believe that there is something unusual about a proctoscopic examination. No one has a patent on proctoscopic examinations. Every general practitioner ought to be able to use a five-inch proctoscope properly, and if he does, he will make a large number of early diagnoses.

The collected statistics show the approximate incidence of malignancy in the colon: cecum, about 6 per cent; both flexures and the transverse colon, about 17 per cent; descending colon and sigmoid, 14 per cent; rectosigmoid, rectum, and anus, 65 per cent. They show a high incidence in the lower rectum which can be seen or felt so easily by proctoscopic or digital examination.

No one knows exactly how many malignancies of the colon arise from multiple adenomatosis, but there is sufficient evidence to show that many of them do. We believe that 100 per cent of these people with multiple polyposis will develop malignancy if they live a normal life span. Therefore, it is important to eradicate adenomas or polyps wherever we find them. We know this simple fact also: that 70 per cent of all adenomas and polyps in the entire colon are found in the rectum, making them amenable to very simple treatment.

I would like now to discuss an unusual case. The patient had hemorrhoids removed, and a diagnosis of squamous cell cancer was made. He remained free from disease, but was sent to us with a secondary nodule in the submucosa. I felt that when there was secondary involvement of the bowel from a squamous cell ma-

lignancy, it probably should be subjected to radiation rather than operation. We treated him with radium, and the disease completely cleared up at this point for a period of fifteen months, when he returned with a nodule identical to that higher up in the bowel. We then felt that we could not radiate this. We did an abdominoperineal operation about a year ago and the patient made a very satisfactory recovery. Thus we cannot believe that all the rules that have been written about squamous cell malignancy of the anus are quite true.

In a group of 137 cases of adenocarcinoma of the rectum, in which we did one-stage combined abdominoperineal resections, there was not a death in the entire series. Bleeding occurred in 87 per cent; diarrhea in 36 per cent—and this is the great group that is being neglected today, for people are more apt to investigate constipation than diarrhea. You see duration of symptoms all the way from three months to twenty months. The lesion is palpable in 87 per cent of the cases. This diagnosis is the simplest and easiest to make. The pathology of the group was as follows: adenocarcinoma, 127; medullary, 3; squamous cell, 2; villous tumor, 4; mucosal polyps were associated with these specimens in 22 per cent.

The bladder gives us trouble in practically all cases, but it is very easily controlled now with the sulfa drugs. The entire hospital stay for this group of 137 cases was eighteen days. Now the hospital time is down to fourteen days.

It was my privilege in 1940 to show you a group of cases involving patients around thirty years of age with malignancy of the rectum and another group of cases over seventy years old. There were 4 cases in the younger group, 3 of which will be discussed below. Ordinarily malignancy in young people is considered a very bad thing. My own feeling has always been that if you diagnose malignancy early in a young person you can do just as much for it as you can in an elderly person. Of course, as a rule, nobody suspects malignancy in young people.

The first patient of this group came to us in 1933. At that time he was thirty years of age. His symptoms were bleeding at stool and diarrhea for eight months. He went to see the family doctor, a great friend, who just couldn't believe that the man was sick; he had always known him as a big, healthy fellow. However, the symptoms continued, and finally he got the diagnosis. When he came to us his red count was 3,300,000 and his hemoglobin was 48 per cent.

I did an abdominoperineal resection. The pathological report was adenocarcinoma of the rectum 3 x 4 inches with invasion of the muscularis and perirectal fat. The glands were negative, however. The patient was discharged from the hospital fourteen days after the operation. He has now gained weight, going from 160 to 230 pounds; he works every day, and also two nights. This man works hard. He worked on a truck for the city; now he is a general maintenance man for a large town. His colostomy gives him no trouble; he doesn't think anything whatsoever about it.

We first saw the next patient in 1939 when she was thirty-two. She complained of pain in the rectum, bleeding from the rectum, and decrease in caliber of the stool. The notes do not show whether it was constipation or diarrhea which was the chief complaint at that time. She says she had constipation. Many of them do, I think, until the tumor ulcerates; then when the tumor ulcerates and becomes secondarily infected, the irritation will produce diarrhea.

We did an abdominoperineal resection almost against her will. She did not feel as though she wanted to go through with it, but finally she persuaded herself that she should. The pathological report was: adenocarcinoma 2 x 3 inches infiltrating all the coats, with extension to the perirectal fat; the glands were negative. She was discharged on the sixteenth postoperative day. She has been well since that time and her colostomy gives her little or no trouble.

The third case is also unusually interesting.

This patient was pregnant at the time she had her symptoms of neoplasm of the rectum, yet examination was not made. She had a bloody diarrhea in the last three months of pregnancy. We know that pregnancy is supposed to have a profound effect on malignancy; in other words, that it is hardly worth while bothering with it. Examination was not made until four months after that, which was seven months from the onset of the symptoms, and at that time she was twenty-six years of age. The complaint was bleeding and diarrhea in the last two months of pregnancy, which continued for three or four months after pregnancy, when examination showed a hard, irregular, indurated ulcer the size of a dollar just at the tip of the finger.

In 1937 I did an abdominoperineal resection. There was an adenocarcinoma $2 \times 2\frac{1}{2}$ inches, with extensive infiltration of the mesenteric fat. Glands, however, were negative. That was nine years ago and she has been well ever since. In 1940 I removed a branchial cleft cyst which was incidental.

Here we have a combination of youth and pregnancy, yet with radical operation she has been well and productive since that time. Her colostomy gives her no trouble at all. She wears a band-aid over it and that is sufficient. It shows how simply care can be taken of some of these colostomies.

I have discussed these cases particularly because there is a shift to the left in treatment of neoplasm of the sigmoid and rectum. I personally went through that a good many years ago and had to take care of a lot of these cases for my older chiefs. I noticed early recurrence locally, which drove me to do something more radical.

Now we again see a tendency to preserve the sphincter. It will take some years to find out

whether that is right or wrong; I know it was wrong before. I think that people are probably stimulated now by the fact that the mortality will be lower in that group because of the use of sulfasuxidine. Personally I have had no experience with it because I have not used any of the sulfa drugs in the preparation of any colon or rectum cases that I have handled. The mortality is about equal to that of others.

At any rate, for the present, I think it is the surgeon's obligation to do the most extensive operation he possibly can. The tendency is to do a small operation for a small cancer and a large operation for a large cancer, which is entirely wrong. It seems to me paradoxical to preach early diagnosis and bring the patient in and then do as small an operation as possible to save the sphincter. We do not do it anywhere else; we always advocate large operations for cancer elsewhere, and yet when it comes to the sensitive matter of whether you are going to preserve the sphincter or not, there is a tendency to do a smaller operation.



Courtesy: American Cancer Society

The Concomitant Diseases or Conditions Associated with Polyarthrititis

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CHRONIC arthritis is not a disease just of the joints, since careful clinical and pathological studies show that a very high percentage of chronic arthritis cases are associated with visceral diseases, which, if properly analyzed, may throw considerable light on the etiology and therapy of rheumatoid arthritis.

My interest in the subject of arthritis dates back many years. In fact, it began immediately after the publication of the epochal papers on the relation of focal infection to chronic arthritis by Billings and Rosenow in 1913. Since then I have been an ardent advocate of chronic infections as causal factors, not alone in chronic arthritis but in many systemic diseases as well. The adherents of the focal infection theory, as you may know, have endured a good deal in the way of sneers and snubs and criticism in the past twenty years. However, the tide has turned; we no longer have to apologize for using the term focal infection or chronic infection. The reason for this change is that within the past few years the results of careful autopsy studies have established that chronic infections

are a very important factor in arthritis as well as in many other diseases.

For instance, we used to be taught, even until the last year or two, that rheumatoid arthritis was wholly different from and not in any way related to rheumatic fever. These postmortem studies show that this is not so; they reveal that in a high percentage of cases of chronic arthritis, changes are found in the heart which are wholly indistinguishable from the changes in the heart in cases of rheumatic fever. It really is astounding when we think that postmortem examinations by reliable pathologists show that 30 to 60 per cent of patients dying with rheumatoid arthritis have cardiac lesions, valvular lesions of the heart, that are identical in every way with the valvular lesions found in rheumatic fever.

These studies have come from Boston, New York, Philadelphia, and Rochester, Minnesota. Perhaps the most comprehensive paper on this subject is entitled "Visceral Lesions Associated with Rheumatoid Arthritis," an article by Philip S. Hench in the *Archives of Pathology* for April, 1943. This was a report based on the *postmortem findings on 30 cases dying with rheumatoid arthritis at the Mayo Clinic; of these 30 cases, 16 showed very definite and*

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typical valvular heart lesions, the same as those found in rheumatic fever. Such findings tend to support, if not actually prove, the contention held by a few clinicians for a number of years, based on clinical studies alone, that rheumatoid arthritis is closely related to rheumatic fever, but with different manifestations because of the difference in the age of the patient and the virulence of the infectious agent.

Equally important as the heart findings was the fact that 19 of the 30 cases at the Mayo Clinic, or almost two-thirds, showed glomerulitis or pyelonephritis, and in one case a kidney stone was present. Furthermore, about 25 per cent of these 30 cases showed peptic ulcer, either active ulcer or the scars of healed ulcer in the esophagus, stomach, or duodenum.

The striking thing is how these postmortems are finally confirming not only what a few of the leading clinicians in the country have thought for a number of years—that the only cause of glomerulonephritis is a chronic infection—but also what many leading gastroenterologists have contended—that a chronic infection is the chief cause of peptic ulcer.

Of course, any tyro in medicine knows or should know that these visceral lesions are not complications of rheumatoid arthritis but that they are concomitant diseases and are all due to the same underlying cause, a chronic infection. If this view is accepted—and the only reason it cannot be accepted would be that men would refuse to accept postmortem findings—is it not rational therapy to remove or to advise the removal of infections to prevent arthritis, and to use prophylactic methods and thereby prevent other very serious visceral diseases as well, diseases of the heart, diseases of the kidney, diseases that kill, and kill early in life? If this is so, is it not advisable for doctors, instead of quibbling over whether they will give gold or sodium salicylate, or will sting a patient with bees, or do something else for joint changes of chronic arthritis—in which case they are just treating one phase of this whole chronic infection problem—to advise as prophylactic



PETER T. BOHAN

procedures, the removal of infections early in life?

IN THE cases which will be reviewed, an attempt will be made to see if there is anything in the history or findings of these patients indicating a chronic infection or recurrent attacks of acute infections. Two of these 4 patients have definite evidence of rheumatic heart disease, such as the pathologists have been finding in rheumatoid arthritis.

Case 1—The patient is a girl, thirty-two years old, single, who was, until nine years ago, a stenographer. Eleven years ago she developed an arthritis of her hands. It then went from one wrist to the other, then to one knee, then to the other. But she continued working for a year, when her trouble became so bad that she had to quit her job. At that time she changed doctors. The second doctor removed her tonsils and in a

month her arthritis had nearly disappeared. She went back to work, and she continued at it for about a year, when, all at once, she had a flare-up of arthritis in her knees and wrists and nearly all the small joints as well as her shoulders. For nine years she has done no work, and has been bedridden most of the time and in pain all the time.

THE general appearance of this girl is that of an advanced case of arthritis deformans, which is merely another name for a case of rheumatoid arthritis which has had bad management. In fact, this girl has not seen her doctors very often because she said they did not give her much hope and did not seem to be interested in her case. Her doctors had probably been reading the literature and had accepted such statements as "the cause of arthritis is not known," "it is a progressive disease," and "there is nothing to do for it." I do not accept any of these statements.

The main feature of this girl's case is the contractures of her joints. Most deformities and limitation of mobility of joints are caused not by bony ankylosis, but by fibrous contracture of periarticular soft tissues and muscles. Most of these joint deformities are due to flexure contractures because of pain. The only satisfactory therapy is prevention. No patient, of course, should be permitted to use pillows under the knees.

In at least 90 per cent of these cases the pain can be controlled by adequate doses of salicylates, either aspirin or sodium salicylate, thus preventing muscle spasm. Also, there is abundant evidence that salicylates desensitize the joint structures, thereby preventing the exudate that is rich in fibrin, which is the "glue" from which fibrous tissue is formed. There is no bony ankylosis of any of these joints.

This patient has been in the hospital under Dr. Russell Haden's care for less than a week. He has used traction on her legs and she thinks her knees are better already. I examined this girl for a few minutes yesterday; she has the typical findings of a mitral stenosis of about

grade II. This is a clue to her having, or having had, an infection in her upper respiratory tract. She was relieved for one year following a tonsillectomy ten years ago. When the arthritis recurred a year later, did she also have an endocarditis?

Another fact of importance is her history of prolonged colds in her head three or four times every winter. This is suspicious evidence not only of recurrent sinusitis but also of improper living habits, such as hot baths and a home that is too hot or too cold. Her appearance indicates inadequate or poorly balanced diet.

Now, in spite of her deformities and disability of nine years' duration, if she will cooperate with Dr. Haden, in six to nine months she should be free from pain, her joints will be straight, and she will be restored to economic independence.

Case II—This patient's trouble began eight years ago, and the doctor gave her some medicine, probably salicylates. At the end of a few months her symptoms had subsided and did not bother her much until two or three years ago. Then it came back in her wrists and fingers.

She presented herself at the Cleveland Clinic two years ago. At that time she complained of pain, stiffness, and swelling of her hands. She also felt exhausted and depressed. Examination showed then, as now, fusiform swelling of the middle joints of the fingers and Heberden's nodes of the terminal joints. Laboratory studies showed a rapid sedimentation rate—it was about three times normal.

DR. BOHAN: You have been coming here for two years, haven't you?

PATIENT: That is right.

DR. BOHAN: You have had more or less trouble with your sinus for some time?

PATIENT: Yes. That dates back about six years.

DR. BOHAN: When did your arthritis come on?

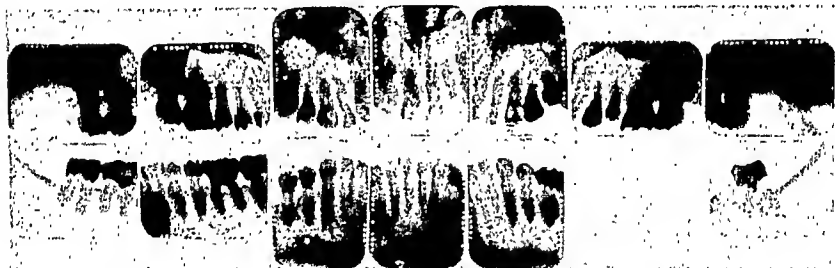
PATIENT: I was troubled with that about eight years ago.

DR. BOHAN: Your antrum was opened and drained about a year ago, wasn't it?

PATIENT: That is right.



Case II-A. These films taken May 25, 1945, show high grade oral sepsis. Following extraction of four teeth with root fillings in the upper jaw and "checking all others," there was no improvement of the arthritis.



Case II-B. This set of films was made October 9, 1946. The findings justify advising extraction of all teeth in the upper jaw and all molars in the lower jaw. Indications are the same as in May, 1945.

DR. BOHAN: Did that influence your arthritis in any way?

PATIENT: I didn't notice that it did.

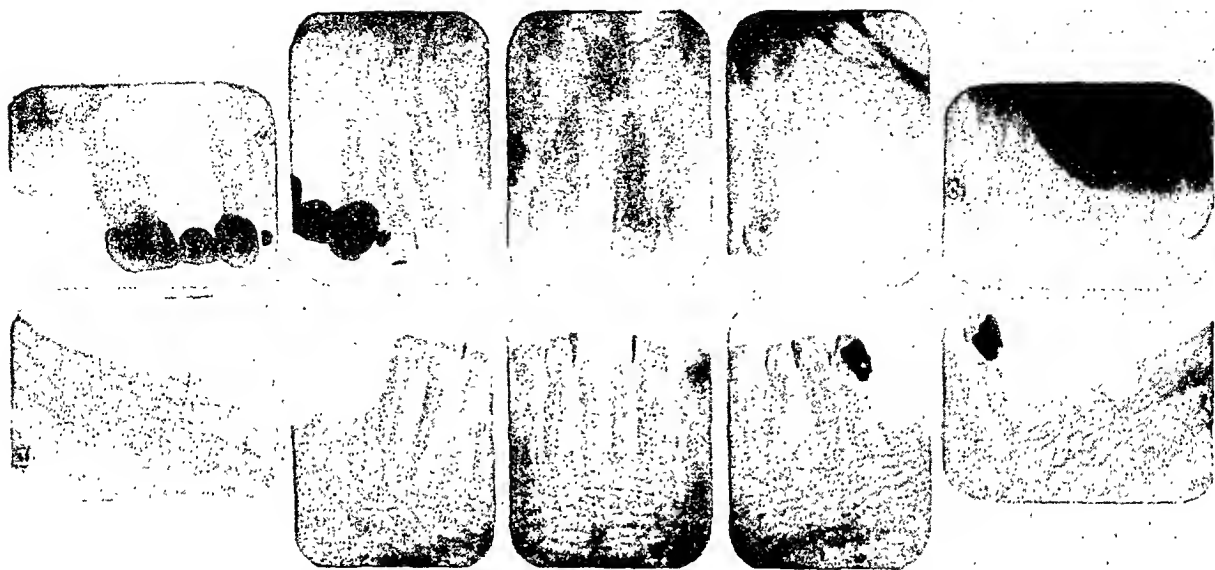
She has an enlargement of the middle joints of the fingers, and what I would like to emphasize particularly is that she has a marked enlargement of the terminal joints of both little fingers and some enlargement of the terminal joints of the other fingers—typical Heberden's nodes.

DR. BOHAN: Do you think the trouble with these terminal joints is due to the same cause as the pain and swelling in the middle joints?

PATIENT: Yes, I think so. It all came on about the same time.

This is the answer we obtain in two cases out of five from patients with such involvement of the finger joints. Of course the changes in the terminal joints are typical of a degenerative arthritis and the spindle-shaped swelling of the middle joints is typical of rheumatoid arthritis. But does it seem logical to assume that the disease of these joints, only an inch apart, is wholly unrelated etiologically?

In my experience, I have never seen a case with bad Heberden's nodes that did not have oral sepsis—not dead teeth, but gingivitis or pyorrhea. It is always easier to tell a middle-aged woman that her Heberden's nodes are due to infections, not senility, and this is my belief.



Case III. From these films it would be difficult or impossible to diagnose oral sepsis, or at least enough to account for all the arthritis this patient has had, and particularly for his cardiac condition. However, as pointed out in the text, the evidence of badly infected tonsils for a number of years is obvious and apparently the sole cause of his arthritis and heart disease as well.

This patient has a number of filled and crowned teeth and marked recession of the gums. I have never seen a patient with false teeth and Heberden's nodes who did not have the nodes first. A year ago Dr. Harris at the Clinic opened and drained an infected antrum without results. Is it not possible that the oral sepsis was a causal factor of the sinusitis? For a number of months this patient has been getting gold shots but her arthritis remains uninfluenced.

Case III—This patient is a traveling man, fifty-five years old. His trouble came on him rather suddenly seven years ago with pain in the knees, hips, back, shoulders, and hands. He had very little swelling of any of the joints; he doesn't know whether or not he had fever. At that time he went to a hospital here in Cleveland and stayed there for two months.

DR. BOHAN: You couldn't walk when you went there?

PATIENT: They carried me in.

DR. BOHAN: How were you when you left? Did they carry you out?

PATIENT: Yes.

DR. BOHAN: Then you went to Florida?

PATIENT: I went to Florida on my back.

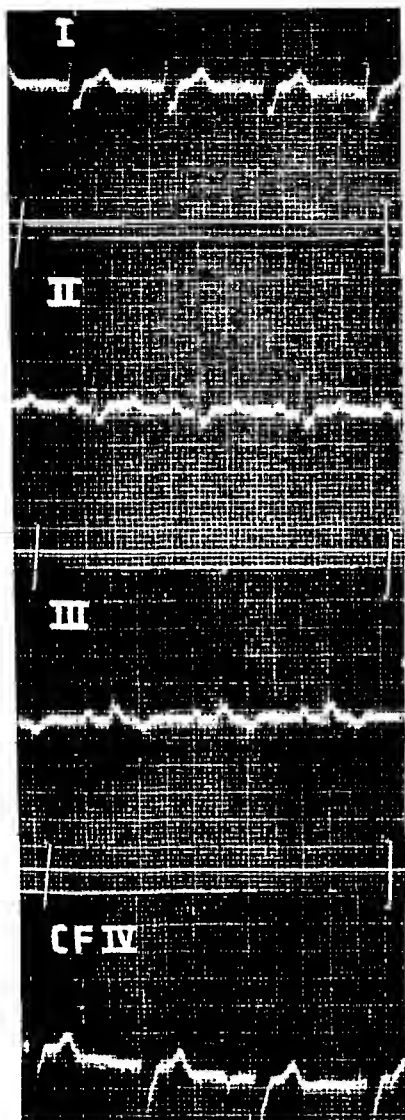
DR. BOHAN: But while you were in Florida you got up and about, didn't you?

PATIENT: In about five months.

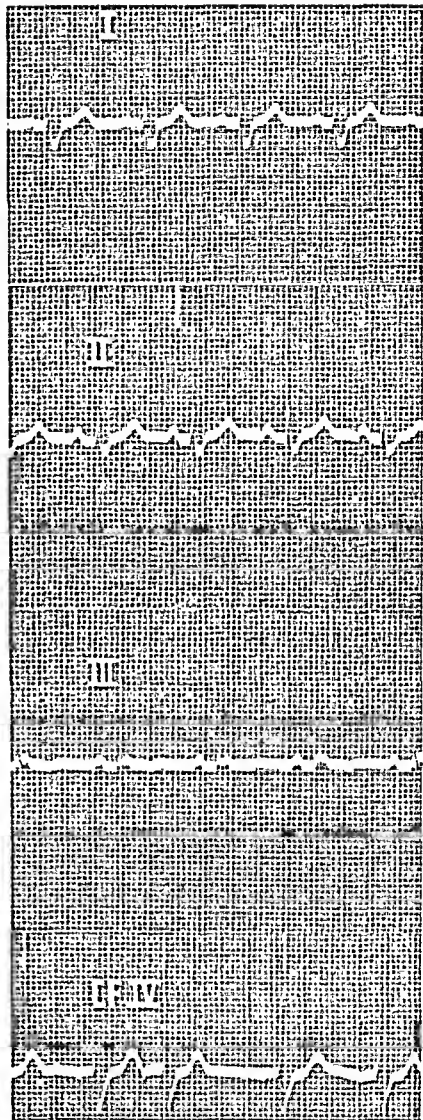
DR. BOHAN: He has been going that way ever since.

There is nothing to find about his joints now. He has no pain or limitation of motion of any of his joints. He explains his gait by saying his ankles are stiff, but examination of his ankles is negative. When asked why he doesn't work he says he is too weak and is afraid he will get a dilated heart.

The more one analyzes this man's complaints the more they sound like functional trouble rather than arthritis. All of his complaints are dominated by fear. Furthermore, he has been getting compensation for total disability for seven years.



Case III. Electrocardiogram taken August 21, 1942, showing right bundle branch block.



Electrocardiogram taken June 4, 1946, showing heart condition unchanged.

WITHOUT a complete physical examination, the diagnosis would have to be psychological rheumatism. Yet examination of his heart shows an apical presystolic murmur and a persistent coupled rhythm. The electrocardiogram illustrated shows bundle branch block, which was found in 1942. Since he has never had rheumatic fever, the diagnosis has to be rheumatic heart disease as a concomitant disease of rheumatoid arthritis. The cause? He insists emphatically he never had tonsillitis or sore throat in his life, but he has marked asymmetry of the tonsils, the right being much bigger than the left. They are both cryptic and he has a palpable gland at the angle of the jaw on each side. This should be enough to establish the diagnosis of infected tonsils. His record at the Clinic shows that Dr. Harris made the diagnosis of chronic tonsillitis in 1945 and again in August, 1946. Thus, if this patient had had a tonsillectomy in his youth he probably would not be totally disabled today.

Case IV—The patient came to the Cleveland Clinic in July, 1935. At that time she complained of recurrent pains in her feet and chest. The symptoms had been severe for six years; in other words, her trouble began seventeen years ago.

After examination and review of the laboratory studies, it was concluded that this was a case of Marie-Strümpell spondylitis. What does Marie-Strümpell spondylitis mean? It is nothing more than rheumatoid arthritis of the spine.

The x-ray pictures are very typical of an ankylosing spondylitis, which, of course, the Sister has. She has a complete obliteration of her sacro-iliac joints accounting for the pain in her legs and the lower part of her back when the trouble began. She has a little trouble in the vertebrae of her neck, as most of these patients have.

What is the cause of the Sister's trouble? The x-ray pictures, according to the interpretation of the roentgenologist at the Cleveland Clinic, show that she has sinusitis.

DR. BOHAN: Don't you have colds occasionally, Sister?

SISTER: I have since March, but not before that.

DR. BOHAN: Anyhow, here is the chronology the Sister herself wrote down: Abscess in her ear when she was two days old; measles when she was three years old; whooping cough at seven; sore throat at ten; influenza when ten with severe nosebleeds. She had a little sinusitis then, didn't she? She had St. Vitus' dance in her twelfth year, sore throat at twelve and again at thirteen, with a high temperature; appendectomy at seventeen with a stitch abscess; phlebitis at eighteen. She had pains in the chest and between the shoulders with temperature when she was twenty-five—bed rest for six weeks. When twenty-six she had severe pains in the hip and leg. Walking was difficult, and this continued for several months. She had a kidney infection at twenty-seven; tonsillectomy at twenty-eight—a little late.

She certainly has a history of infections—enough to account for her spondylitis, as well as the kidney infection and chorea.

DR. BOHAN: Are you any better than you have been, Sister?

SISTER: I am some improved.

DR. BOHAN: But you are in pain most of the time?

SISTER: Yes, Doctor.

DR. BOHAN: But she works every day. You teach every day, don't you, Sister?

SISTER: Yes, I do, Doctor.

DR. BOHAN: In conclusion I would like to tell you of a patient I saw in an Army camp three years ago. I was invited to come down there and discuss the subject of arthritis. When I finished, a young colonel thirty-eight years old, head of the surgical service, came to me and asked if I cared to hear his personal experience with spondylitis. I naturally told him I did. I will give you his story briefly.

He began by saying, "Five years ago tonight I was on the flat of my back in bed with a plas-



Case IV. Film of cervical spine shows calcification of the spinal ligament between the last cervical and the first dorsal vertebra.



This film shows destruction and ankylosis of sacroiliac joints. Generalized atrophy and calcification of spinal ligaments with bulging at intervertebral areas in lower dorsal and upper lumbar regions. Bamboo spine.

ter of Paris cast from the middle of my thighs to my neck." He continued by saying that after tolerating this torture for five weeks, sleeping two hours out of twenty-four, he told his doctors that unless they took the cast off he would kill himself. The doctors realizing that he meant what he said, took off the cast. He then proceeded to treat himself and at the end of one year returned to work and has worked night and day since.

I then naturally asked him what his treat-

ment was. He said, "Aspirin and not another thing—90 grains every day for 365 days and 90 grains twice every week since." He returned to work four years ago.

After complimenting him on his intelligent management, I then asked if he thought he got sick in the first place because he had not taken aspirin all his life. He said, "I know exactly what you mean. I am having them out one or two a month, and in a short time I expect to have complete dentures just as nice as yours."

DIAGNOSTIC CLINIC

The Differential Diagnosis of Low Back Pain

MAXWELL HARBIN*

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Low back pain is a very frequently encountered problem and one which I know you all see at one time or another. We orthopedic surgeons see these patients all too often ourselves, perhaps because almost 50 per cent of our patients today seem to be those with low backache, and many of them with pain down the leg, either in the front or back or on the side.

In the problem of low back pain, one of the most important things is a complete history. A complete physical examination should be done on all these patients. I would emphasize that the patient should always be completely disrobed. We shall assume that the examination has eliminated the genito-urinary organs as a factor in the production of symptoms. The mode of onset of low back pain is of considerable importance. This should be determined accurately from the patient.

The presence of an injury, sufficiently severe to produce some pathologic change capable of causing pain in the back, must be

obvious. In cases in which the question of compensation arises, the accuracy of the description of the injury may be questioned. These cases are always difficult to handle, and it is often necessary for the physician to judge the honesty of the patient.

Insidious onset may apply to a multitude of conditions. In fact, most conditions which produce backache, with the exception of those which are included under the heading of trauma or traumatic spondylitis, may have an insidious onset.

The type of pain is a most important point to determine. In many cases in which the pain is constant it may be difficult to decide what importance to attach to the patient's description of the pain. However, many patients give a definite history of pain which is brought on by activity and which is relieved by rest. This type of pain has been called static. Many cases belong to this group. In general, a pain in the back is more likely to be the result of traumatic or hypertrophic arthritis, but occasionally it may be caused by postural strain. In cases which give a more or less opposite history, the condition may be considered infectious in origin. In this group the patient gives a definite history of pain which is noted particularly

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after resting and upon arising in the morning. Such pain wears off after activity. These two groups of symptoms may be combined in some cases. It cannot be said that any hard and fast rule or conclusions can be drawn from these facts, but they are, however, helpful in sizing up a case.

WE SHALL proceed with two cases. We shall not have enough time to consider the more unusual types of low back pain caused by tumors of the lumbar spine and pelvis, nor metastatic tumors in the same region, nor the rarer types of infection such as osteomyelitis, actinomycosis, typhoid, brucellosis, or gonorrhea.

We must, therefore, limit ourselves, unfortunately rather briefly, to the common postural type of backache, the congenital anomalies such as spondylolisthesis, unstable back, trauma, acute and chronic fractures, and the sprains, the so-called strained back, post-traumatic neuroses, and radiculitis, which, you know, is so popular today, referred to as rupture of the nucleus pulposus. We may also briefly mention the ependymal adhesions of the cauda equina and peridural varicosities. Time does not permit a discussion of the diseases of the spine such as arthritis and tuberculosis, but I hope to make a few remarks about fibrositis.

The history is of tremendous importance in the differential diagnosis of low back pain. The first patient is a female, forty years old, who was well until six months ago when she developed, without known cause, a dull pain in the low back, radiating down the posterior left thigh, with pain quite acute for two weeks; it was considerably relieved by rest in bed. The pain was not associated with any known trauma.

Six weeks ago the pain extended into the lower leg and into the sole of the left foot. She also noted some numbness of the sole of the foot; sneezing and coughing aggravated the pain. She has been in the hospital several days.



MAXWELL HARBIN

She tells me that rest in bed has not relieved her symptoms.

The patient, when possible, should be examined with the clothing removed, and the contour and position of the back noted. Motion is of great importance, as well as posture. This patient stands with a moderate lordosis, and with the left knee slightly flexed, and that is of significance.

We are interested in forward motion as to whether there is limitation, and to what degree. When the patient bends forward, mobility is relatively good, and there is motion in the lumbar spine up to seventy per cent of normal. Flexing to the left is painful and is of significance in this particular situation. Hyperextension of the back is also painful. As you will recall, there has been no history of injury.

I wanted to demonstrate to you the ordinary tests that we do for these back cases. Points of tenderness are important, particularly the constancy of these points of tenderness: (1) whether there is tenderness in the lumbosacral region; (2) whether it is central between the

fifth lumbar and the sacrum, or whether it is to one side or the other.

FURTHER SYMPTOMS

THE patient has no tenderness in the lumbosacral region. She has tenderness over the fascia overlying the sacro-iliac. I am not palpating the sacro-iliac synchondrosis; it cannot be done. One merely palpates the fascia over the posterior ilium; the joint is two or three inches below. She has tenderness over the entire left sacro-iliac fascia, not the joint.

Another point of importance is the matter of tenderness over the posterior superior spine of the ilium. She has no tenderness whatever except over the fascia overlying the left sacro-iliac. Sacro-sciatic notch tenderness is very important, particularly in radiculitis. She has no sacro-sciatic notch tenderness on either side. Turning over on the back is painful.

All that we have so far in the way of positive signs is some pain on hyperextension of the back, tenderness over the left sacro-iliac fascia, and pain on flexing toward the left side of the body. A so-called Lasèque's sign or straight-leg raising test should be done. This consists of extending the leg with the knee completely extended; when pain along the back of the thigh occurs, it is known as a positive test. It occurs in various types of radiculitis.

Flexion of the left hip is painful at 35 degrees. There is no pain on right straight-leg raising. The reflexes we will not take the time to go over. Her knee jerks and ankle jerks are normal. She has no gross sensory change. Her roentgenograms are negative.

How are we to identify this condition? There is no history of injury. She merely has tenderness over the left sacro-iliac fascia, but she does have a characteristic type of radiation of pain down the posterior thigh along one of the elements of the sciatic nerve, and the pain on straight-leg raising is suggestive of radiculitis in association with tenderness. Frequently, however, tenderness is present in radiculitis over the lumbar spine, the fifth,

commonly, sometimes the fourth, usually toward one side or the other. I think we have to conclude that this patient has a mild radiculitis, and the most common cause of that, as you know, is herniation of the nucleus pulposus, which in her situation, with radiation of pain to the sole of the foot, would suggest the fifth somatic level, that is between the fifth lumbar and sacrum.

However, that cannot be absolutely determined, since her signs are not entirely typical, but must be left to treatment. If the pain becomes more severe, if she has more disability, and if the usual conservative measures fail to give her relief, then it will be necessary to carry out opaque intraspinal studies for determination of the site and degree of the lesion.

The second patient, male, thirty-four years old, has a most extraordinary story. He had no difficulty until four days ago. Eight hours before he came into the hospital he was pulling up some tree roots, bending over naturally, when he felt something suddenly give in his back. The pain and resulting numbness in both legs was so severe that he could not walk from the place he was standing—a sudden onset. The pain radiated down both legs posteriorly, and the numbness, which was rather diffuse, lasted for a short time. He was unable to straighten up. On his admission to the hospital he had a slight list to the right, with muscle spasm and general tenderness over the fourth and fifth lumbar spines and both sacro-iliacs.

We shall discuss a few points in regard to a patient with acute onset of low back pain and leg pain in contrast to the patient just described with the gradual onset of not so severe a degree.

The second patient moves with much more caution, and that is of great importance. In contrast to the other patient, he has a straight lumbar back. That is very significant and is commonly associated with irritative lesions of the low lumbar spine. One should also inspect the back for a list toward the right or left. Not always, but frequently patients list away from the side of pain.

His lumbar back remains straight when he bends over and keeps his knees straight. He says it is painful. It hurts in the lumbosacral region. The back is quite limited in bending to left and right. When he bends backwards, he has good hyperextension.

With the patient lying face down on the table, palpation shows that he has tenderness in the lumbosacral region. When he came into the hospital he had complete loss of both knee jerks and ankle jerks. In forty-eight hours he had recovered these reflexes. His pain had lessened. There is now no pain or tenderness over the posterior superior spines of the ilia. The patient should always be relaxed when palpating for points of tenderness. There is no tenderness over the sacro-iliac fascia and no sacro-sciatic notch tenderness.

There is pain at 35 to 40 degrees on left straight-leg raising. During the first day in the hospital he would only allow 20 degrees, and the same on the right side, rather symmetrical. Both knee jerks and ankle jerks have returned. This patient demonstrates a condition with acute onset, with obvious sudden irritation of certain elements of the cauda equina. His roentgenograms are entirely normal.

One must assume that for such a condition to have cleared so rapidly he must have had a large disruption or protrusion of the posterior portion, probably of the annulus fibrosus or the intervertebral disk. Bed rest and traction, which he had, must have resulted in the disk's slipping back. It does happen. These disks change position frequently. That is the reason these patients have a history of recurrence of pain, a period of freedom, and a period of recurrence which may be acute or mild.

I would cite one point in the differential diagnosis of low back pain, namely, the use of novocain. In patients in whom one suspects the possibility of a focal fibrositis in contrast to irritation of elements of the caudal roots or the sciatic nerve, it is wise to infiltrate those so-called trigger points with novocain to eliminate that as a factor of pain. In fibrositis of the low back (and it is not uncommon, but at times rather difficult to differentiate from a

radiculitis) this novocain test serves two purposes: it aids in the differential diagnosis of the cause of low back pain, and also, in perhaps 50 per cent of patients with fibrositis, gives relief. Remember that with fibrositis of the low back, particularly the focal type, there may be radiation of pain down the posterior thigh, but it rarely goes below the mid-thigh. When pain goes below the mid-thigh or below the knee, fibrositis is not the causative factor; there is something of a deeper character resulting in nerve irritation.

The pain which flows from the low back fibrositis is the result of muscle spasm. It may be beautifully demonstrated in the so-called fibrositis of the elbow or so-called tennis elbow where just below the lateral epicondyle the point of tenderness is situated and the pain flows down the forearm. The same thing happens in the low back.

When this process is focal, it can largely be determined by the use of novocain at the trigger point. This patient had novocain injected in the tender point, namely, the lumbosacral fascia or ligament. He received much and rather quick relief from pain, but at the same time had the reflex changes, the sudden onset, the symptoms of numbness and pain down the leg, all of which were very definitely pathognomonic of an irritation of certain roots, certain of the caudal trunks in the low lumbar spine.

This subject is a very broad one and is very important from the standpoint of many types of patients, both from an industrial standpoint as well as the ordinary private patient's relief of his disability. I would, above all else, like to re-emphasize these points in differentiation of these low back conditions, namely the need for a thorough chronological history; inquiry as to the element of force applied initially; location of the constant points of tenderness; a thorough physical examination; also, in a certain number of cases where there is radiation of pain down the leg, a complete neurological examination, and always roentgenograms of the lumbo-sacral spine to exclude such diseases which are visible in the roentgenograms.

EDITORIALS

REPLACEMENT OF THE COMMON DUCT

THE REPAIR of an accidentally incised, ligated, or clamped ductus choledochus within a few days of its occurrence usually is a simple matter for the seasoned surgeon. The replacement of the common duct (intra-abdominal biliary fistula) will try the soul of the most skilled. Much misleading and footless surgical argumentation would be forestalled if the facts and conceptions concerning the repair of a common duct—and also the construction of a synthetic common duct—were carefully kept in their respective technical pigeonholes. Much of the literature on common duct reconstruction the past thirty years has produced more heat than light as is customary with surgical problems during the groping for solution. The problem has not as yet been adequately solved.

An outstanding contribution to the tools and artifices of common duct replacement was revealed in the March, 1947, issue of *Surgery, Gynecology and Obstetrics*, by Dr. J. G. Montgomery of Kansas City, Missouri, who relates his successful experiences with the "Use of Umbrella Catheter To Produce Internal Biliary Fistula."

The bulbous end of the catheter prevents the too early passage of the tube, thereby insuring its retention for the all important time interval during which a reasonably dependable fistulous tract becomes fabricated. The crux of all rubber or metal tube operations of this type is the transcendent time interval. How long should the tube remain? How long is long enough?

In healthy experimental animals, with normal tissues—with prompt recoveries from aseptic procedures—with early feedings and adequate fluids, and concomitant normal biliary outputs—the rubber tube needs remain in situ but five days. Per contra, for the debilitated individual with deep jaundice—with electrolytic imbalance—with protein deficiency—with an anxiety overlay—and with the available reconstruction tissues impregnated with antagonistic biliary salts—the required time interval for the successful production of an internal biliary fistula, is a matter of many weeks of skilled post-operative management.

Despite the recorded successful cases in which the tube passed prematurely, much attention has been given to methods by which this may be prevented. Dr. Charles H. Mayo devised and successfully employed rubber tubes which were manufactured with an irregular external surface, so that the encircling tissues would grasp the outer walls and prevent the too early extrusion of the tube into the bowel. A cuff of rubber, turned down on the end of a pure rubber tube serves dependably, although the cuff slightly narrows the underlying lumen of the tube. The umbrella catheter, as suggested by Dr. J. G. Montgomery, has the advantages of: (a) being procurable in pure rubber; (b) being available in acceptable calibers; (c) immediate accessibility in most hospitals; and (d) having a bulbous perforated end.

The writer plans to utilize on the next duct replacement case, a pure latex umbrella or mushroom type of catheter such as successfully employed by Dr. J. G. Montgomery—although probably he shall be tempted to amputate most

of the "mushroom" and depend on the resultant finger-shaped tip to retain the catheter in situ for an adequate interval. It does not require much resistance for the retention of this fistula-producing tube, if the distal end is not permitted to project more than three to four inches into the duodenum.

The writer concurs in Dr. Montgomery's opinion that the present available Vitallium tubes have many disadvantages, not outweighed by their acceptability by the contact tissues, nor their larger bore versus outside diameter, compared to pure rubber tubes. The great number of patients who have worn latex T tubes in their common ducts for months or years, negates most of the arguments for Vitallium tubes so far as concerns the alleged irritability of pure rubber tubes used in duct replacement procedures.

It is doubtful that a T tube should ever be employed in the replacement of a common duct. It is one thing to remove a T tube from a sturdy original common duct which has required drainage for a protracted interval. It is quite another thing to drag from a tenuous fistulous tract, the tearing angular wedge of rubber, as many surgeons have regretfully discovered.

Failures in this work have been encountered as a result of infection of the fistulous tract occasioned by the use of a T tube. It is well recognized that most fistulous tracts following cholecystectomy, for instance, become infected if the drainage tube is not removed within five days. A common duct with a T tube inserted for prolonged drainage can "take it" so far as concerns infection which follows down the limb of the tube projecting through the skin surface. This is not the case with the less resistant tissues upon which one must rely in the production of a fistulous tract, and it is a recognized cause of failure. Some failures are occasioned by the inadequate output of bile following the decompression of the liver in those cases which have complete biliary obstruction. Some patients have been operated on after the liver has "died" so far as concerns re-

sumption of function. Biliary pressure is the most important factor in the maintenance of so-called permanent biliary fistulae. Abundant bile output is of the greatest importance during the many weeks required for the establishment of a synthetic common duct.

Fortunate is the unlucky individual whose common duct mishap results in an external biliary fistula rather than a healed duct stump and an intense jaundice. The surgical preparation of such a patient is quite simple. That required by the chaotic physiological chemistry in the patient who for many months has had no discharge of bile, demands meticulous attention to the protein, sugar and electrolyte balances.

PATIENTS who require common duct replacements are *not* emergency cases. Special preparatory medical treatment is needed. They should not be operated upon by the average surgeon. Many die who fall into hands which may brilliantly perform a thyroidectomy or a hysterectomy. While the operation itself is quite simple, there frequently is a great amount of exacting dissection required to separate the agglutinated tissues in the average case; because of the race against time this is an agonizing procedure on a patient who is precariously near the edge. An unusual anatomical erudition is requisite for the baffling problem of locating and identifying the proximal stump of the common duct in the shortest time. This is true even in those simpler cases in which a so-called persistent external biliary fistula is present. These non-jaundiced patients can better withstand the inescapably lengthy exploratory procedure, because they can be more assuredly fortified for severe surgery, than can the individual who has had complete biliary blockade of long duration.

Should one question the complex and exacting problem of modern, laboratory-checked, adequate preparation of an acholic patient for surgical exploration, a review of the excellent article entitled, "Management of Jaundice Patients," by Dr. Albert M. Snell of Rochester,

Minnesota, in the April 19, 1947, issue of the *Journal of the American Medical Association*, should convince the doubter as to one's moral responsibility in the surgical preparation of the victim of choledochus blockade. Not all cases of common duct occlusion following surgery are due to surgical accidents. A phlegmonous process which can cause gangrene of the gall bladder can also extend via thrombophlebitis and destroy the common duct. Slow asymptomatic cicatricial contraction of tissues following surgery on or near the common duct can produce occlusion, which usually becomes evident within sixty days.

Replacement of the common bile duct is no field for the tyro, nor for the opportunist. Patients with long-standing jaundice following surgical procedures in the vicinity of the common duct should be referred to men whose clinical souls have been scarred with defensible surgical disappointments, and who have thereby learned the most dependable solutions for this disastrous pathology. Even in their seasoned hands, the percentages of failures and deaths will be high—but those who died shall not have died in vain.

A.G.S.

RELATION OF BLOOD GROUPS TO DISEASE

MANY efforts have been made to correlate the human blood groups with various syndromes of uncertain etiology. The discovery of the workings of the Rh factor has given hope to these undertakings, because the Rh factor produces erythroblastosis fetalis only by crossing the placental barrier. If one antigenic system can give rise to pathology, there is little objection to the belief that others might do so. However, attempts to find other similar conditions have not been particularly successful.

Bakwin and Wiener have reported a study in the *Journal of Pediatrics* for January, 1947, on 23 patients with congenital athetosis, who had had icterus gravis during the neonatal period. Icterus gravis may result from Rh or A-B sensi-

tization, as well as from other causes. Hence, the investigators sought to determine whether the athetosis might not also have been caused by the blood group incompatibility. Upon testing the bloods of parents and children, the investigators decided that the Rh and A-B factors could not have been the cause of the congenital athetosis in the majority of patients.

In another investigation, Jungeblut and his associates attempted to correlate blood groups with the occurrence of poliomyelitis. Their findings, published in *Annals of Internal Medicine* in January, 1947, suggest that persons of blood groups O, A₂, and "non-secretor" types suffer paralytic involvement in poliomyelitis more often than might be anticipated from the proportions of these types in the population. Likewise, "secretors" and persons of group B are less frequently affected than might be expected. Paralytic patients show a frequency of blood group A₁ that is essentially the same as that of the normal population.

C.R.

TOOTH DECAY AND VITAMIN DEFICIENCY

FOR several years now, physicians and dentists alike have discussed and disputed the possible relationship between tooth decay and vitamin deficiency. Many investigators have maintained that tooth decay is caused, at least in part, by an insufficiency of vitamins in the diet. Other students of the subject have taken an exactly opposite view—have held, in fact, that persons with properly balanced diets are more susceptible to tooth decay. A recent study conducted at the Hillman Hospital, Birmingham, Alabama, by Mann, Dreizen, Spies, and Hunt, should throw light on the question.

These investigators who reported their work in the February 15, 1947, issue of the *Journal of the American Dental Association*, demonstrated that malnourished persons have less tooth decay than well-nourished persons. They had as their subjects 233 patients. Several different tests for dental caries and vitamin de-

ciency were performed on each patient. Furthermore, the patients were carefully examined clinically for any evidences of malnutrition. Of the group, 124 showed evidence of nutritional deficiency diseases. There were actual lesions caused by malnutrition, or chemical examinations revealed low blood vitamin levels. The remaining 99 patients presented neither lesions nor low blood vitamin levels; they appeared to be well-nourished.

The 124 poorly nourished patients had an average of 2.07 tooth surfaces decayed, 1.60 teeth missing, and 0.96 tooth surfaces filled. The 99 well-nourished patients had a much poorer record. They averaged 3.21 tooth surfaces decayed, 2.23 teeth missing, and 9.75 tooth surfaces restored.

Obviously, therefore, the poorly nourished group had much less dental decay than those on adequate diets. Actually, the malnourished persons had on the average only about one-third as much evidence of tooth decay as did the well-nourished individuals. However, the poorly-fed persons had much more pyorrhea than did the well-nourished.

R.W.C.

HOW TO USE LANTERN SLIDES

WORDS are the means we have for conveying to other persons a picture that is in our own mind. If we can show them the picture directly, so much the better; we save a great many words, and words and picture act to drive each other home. There is a double chance that our material will be remembered, for it is reaching the brain in two ways, by eye and ear. From the audience's point of view, this double channel eases the strain of concentration, insuring a correct interpretation of the picture in the lecturer's mind.

Lantern slides are thus a great adjunct to a lecture whenever their material is directly pertinent, and it is worth while taking pains to

realize this advantage to the fullest. So many otherwise excellent talks are reduced to 25 per cent effectiveness by poor handling of slides that it may be helpful to list a few common-sense do's and don'ts in their use.

If you want to hold the attention of your audience:

1. Coordinate your slides carefully with the text and arrange them in proper sequence. If not of a sort to be coordinated they should be shown all together, usually after the lecture, not during it.

2. Leave each slide on the screen long enough for the audience to comprehend it; discuss it appropriately, and then remove it.

3. Slides should be easily legible even from the rear of the room.

4. Some slides present evidence, some conclusions. There is a proper place for each.

5. Know your slides well enough to discuss them without turning your back on the audience.

6. Use a pointer to gain clarity and emphasis.

What not to do:

1. Don't leave a slide hanging on the screen while you talk about something else.

2. Don't try to get too much on one slide. It is a picture, graph, or chart, not a book.

3. Don't read the slide to your audience. They can read.

4. Don't talk to the slide; talk to the audience.

5. Don't scratch the screen with your pointer. If electric, don't flash it around the room, and don't let it play on the screen except when in use.

6. Don't call for the next slide before you have discussed the one on the screen.

7. Don't change slides too rapidly. Give each one a chance to sink in.

8. Don't use slides at all unless they are good ones. Better a good talk without slides than a potentially good talk interrupted by poor slides.

R.O.

This Month in Medicine

PELLAGRA

THE cause of pellagra has been a subject of scientific dispute for hundreds of years. And it is not yet settled. Although many modern writers assume it to be caused by a deficiency of nicotinic acid in the diet, others have marshalled substantial proof that pellagra is caused by a toxic principle in corn.

Recently, Raska has proposed that adenine, a constituent of many physiological catalysts, may be responsible for pellagra. This investigator believes that the proper regulation of the concentration of free and bound adenine in tissues and body fluids is of considerable importance to the animal economy. He disturbed that regulatory mechanism by feeding large quantities of adenine to dogs and rats. In this manner, he interfered with the normal metabolism of adenine-containing substances, vitamins, hormones, and enzymes. As a result, the animals developed pellagra-like lesions, characteristically observed in experimental avitaminosis.

Raska believes that the adenine combined with the vitamins, particularly those of the B-complex, and thereby prevented their utilization by the animal. If similar mechanisms occur in human beings, the elimination from the diet of foods containing adenine, in a form that leads to avitaminosis, may bring a reduction in pellagra. At any rate, Raska has undertaken an analysis of the adenine content of certain foods.

SUGGESTED READING

EDITORIAL: Pellagra and corn. *Nutrition Reviews*, 3:267, September, 1945.

WOOLEY, D. W.: The occurrence of a "pellagrogenic" agent in corn. *J. Biol. Chem.*, 163:773, June, 1946.

RASKA, S. C.: The production of experimental pellagra by adenine. *Science*, 105:126, January 31, 1947.

CRUTCH MASTERY

MOST scientific articles describe techniques, principles and practices. Once in a great long while an article appears that yields human understanding. Such is the anonymous article entitled "Crutch Mastery," which appeared in a recent issue of the *American Journal of Surgery*. The author, a physician and victim of infantile paralysis, discusses his fifty years of personal experience with a crutch. It makes good reading, for it is lively, informative, tinged with humor and pathos.

Every physician, every crutch manufacturer or user can profit by reading this article. It is packed with practical suggestions on the use of the crutch, in a variety of environmental situations. The author wades the swiftly flowing waters of a trout stream, alights from moving trains, dons a Beebe diving helmet and negotiates the bottom of a lake, plays golf and tennis, even ascends in a balloon. Whoever he is, the author is a real man.

SUGGESTED READING

ANONYMOUS: Crutch mastery. *Amer. J. Surgery*, 73:404, March, 1947.

TISSUE CULTURE

ALTHOUGH tissue culture work has progressed for many years, seldom has it been applied to clinical investigations. Some authors, however, have suggested its value in the diagnosis of tumors.

Recently, Grace has reviewed the literature of the subject and made some further comments from his own experience. He points out that tumor cells, particularly atypical cells, can be identified more readily by tissue culture methods than by section-

ing. Normal tissue does not proliferate from a single cell, whereas malignant tissue does. Because of this difference in the two types of tissue, an early diagnostic procedure might eventually be developed. Furthermore the degree of malignancy of a tumor cell is proportional to its activity in tissue culture. If the cells are very active, the patient is in danger. The author believes that tissue culture methods should always be used in the diagnosis of Hodgkin's Disease, for with this technique the nodules of this disease can be differentiated from other lymphomas.

SUGGESTED READING

SANO, M. E., and SMITH, L.: Tissue culture as a diagnostic aid in the identification of atypical tumors. *Arch. Path.*, 30:594, 1940.

GRAND, C. G.: Tissue culture studies of cytoplasmic inclusion bodies in lymph nodes of Hodgkin's Disease. *Proc. Soc. Exper. Biol. & Med.*, 56:229, 1944.

GRACE, F. J.: Tissue culture as a clinical aid in the diagnosis of malignant tumors. *Amer. J. Surg.*, 73:326, March, 1947.

ABORTIFACIENT ACTION OF
PENICILLIN

RECENT reports have pointed to the possible abortifacient action of penicillin. Four groups of investigators have treated with penicillin a total of 90 pregnant women, most of whom were being treated for syphilis. In this group there were 6 abortions and 13 threatened abortions. Two other groups of investigators administered penicillin to 180 syphilitic pregnant women without a single abortion or threat of abortion. These latter investigators, therefore, do not believe the drug has an abortifacient effect.

In a recent review of the subject, Rainie and Chapin suggest that these discrepant findings may result from impurities in certain commercial penicillin preparation—impurities that have echolic properties. When one considers that ergot is a fungus, just as is penicillium, the suggestion does not appear far-fetched.

SUGGESTED READING

RAINIE, R. C., and CHAPIN, M. A.: Abortifacient action of penicillin in pregnancy. *J. Maine Med. Assn.*, 38:23, February, 1947.

EFFECT OF LEMON JUICE ON TEETH

SOME years ago lemon growers and distributors initiated a national advertising campaign designed to promote the sale of lemons. One of their most potent ads proclaimed the virtues of drinking a solution of lemon juice and water, immediately upon arising in the morning. The public did as it was told. Result: Teeth were dissolved by the acid solution.

Stafne and Lovstedt, of the Mayo Clinic, have found that the increased and injudicious use of lemon juice has caused considerable tooth trouble. The teeth become hypersensitive to temperature changes and to hygroscopic substances. Stains and stain lines are absent. Fillings project above the surface of the teeth—the best diagnostic aid. The degree and rapidity of decalcification varied from person to person, depending probably upon differences in amount and buffer capacity of the saliva.

The authors, recognizing the vitamin C content of lemon juice, suggest that if it be used as a therapeutic agent, it should be taken with meals, and not in too great concentration. In other words, lemon juice like all other highly touted panaceas, is easily misused.

SUGGESTED READING

STAFNE, E. G., and LOVSTEDT, S. A.: Dissolution of substance of teeth by lemon juice. *Proc. Staff Meet., Mayo Clinic*, 22:81, March 5, 1947.

TOTAL INTRAVENOUS
ALIMENTATION

FOR many years physicians have recognized the desirability of a complete intravenous diet. Only with the development of protein hydrolysates, however, has total intravenous alimentation become possible, and practical. Bigham and his associates point out the many uses of a mixture of protein hydrolysate, glucose, salt, water, and vitamins.

Preoperative and postoperative intravenous feeding has been found of great value in operations for carcinoma of the bowel, in gastric resection, and when intestinal fistulae are present. The gut was found to be small, of good tone, easy to han-

dle and free of contents. Patients were free of post-operative distention and discomfort. In operations for hemorrhoids, where the surgeon desired a temporary cessation of bowel movements, the intravenous method of feeding has kept the patient free of hunger and abdominal distress. Unless there are intestinal lesions of some sort, stools usually cease within two or three days after initiation of intravenous alimentation.

The investigators insist upon total, not partial, intravenous feeding, if the desired result is to be obtained. Further, the treatment must be initiated several days preoperatively, and then used only when indicated. Debilitated surgical patients and those with violent infections are obviously candidates. The treatment is contraindicated in renal insufficiency, hemorrhagic shock, imminent heart failure, and probably severe liver damage.

SUGGESTED READING

BIGHAM, R. S., et. al.: Total intravenous alimentation, its technics and therapeutic indications. *South. Med. J.*, 40:238, March, 1947.

CHEMICAL CORPS MEDICAL RESEARCH

MEDICAL progress, made by members of the Armed Forces, is usually under the direction of the Medical Corps. But still another branch of the Army, the Chemical Corps, has also to its credit several significant medical discoveries or developments. Recently, the Chemical Corps has been drafted to take part in the national cancer program. Its job will be the testing of new compounds for the treatment of cancer.

The Chemical Corps already has initiated a most promising line of research. The war gases known as "nitrogen mustards," acquired after the fall of France, have been given intensive study. They are peculiar in that although they are poisonous to nearly all parts of the body, they are particularly destructive to bone marrow and lymph glands. This interesting affinity suggested their

use in the treatment of leukemias, Hodgkin's disease, and lymphosarcoma. Initial trials, made by several investigators, indicate that these compounds may be of especial value in the treatment of Hodgkin's disease, relief having been afforded to patients with this disease, who no longer responded to x-ray.

Although only three nitrogen mustards have been investigated as a treatment for cancer, there are over sixty more of these compounds that may yet be tested. It is not unreasonable to expect that these studies will uncover some interesting and useful drugs.

Most physicians are unaware of the fact that the Chemical Warfare Service was largely instrumental in the development of penicillin aerosol therapy of the lungs and bronchi. CWS interest was generated by the necessity of protecting the soldier from smokes and gases, many of which actually are aerosols. In the course of the investigations, attention was given to the feasibility of bringing biologically active materials, chemotherapeutic agents and antibiotics, into the lungs by means of the aerosol technique.

That the Chemical Warfare Service should properly be interested in these possibilities can be readily understood when one considers that during the war bacteriological as well as chemical warfare were subjects of great importance. As a result of studies by members of the Chemical Warfare Service and associated groups, penicillin aerosol therapy was found to be a practical clinical procedure. Penicillin combined with streptomycin or hydrogen peroxide, in aerosol form, has been found of value in the treatment of both tuberculous and non-tuberculous pulmonary suppuration. Further studies in this field will be awaited with great interest.

SUGGESTED READING

Wood, J. R.: Chemical corps joins cancer crusade, *Chem. Corps J.*, 1:30, January, 1947.

Abramson, H. A.: Principles and practice of Aerosol therapy of the lungs and bronchi, *Ann. Allergy*, 4: 440, November-December, 1946.

R.W.C.

MEN OF MEDICINE

PROBLEM CHILD OF MEDICAL MEN

STARTING his life as a "dead end kid" in an Irish neighborhood of old Newburgh in suburban Cleveland, Dr. John Augustus Toomey still bears in his personality the marks of early battles. Tall, red faced, with bristly hair, he has always known how to stand on his own two feet and give as well as take it on the chin. If he thinks the scientific theory of a colleague is wrong he can deliver a verbal punch straight from the shoulder. Yet his chief hobby is helping a medical student, an employee, the parent of a patient, or whoever comes along to solve a tough financial or personal problem.

Were it not for his intellectual honesty, mixed with a generous portion of belligerence, Dr. Toomey, at the age of 58, might today be a successful attorney, judge or holder of an important political office. After his graduation from John Carroll University, he studied law at the Cleveland Law School and received his law degree in 1913. He entered as a partner in practice with a young attorney who later became a prominent judge.

But to the astonishment of his friends and colleagues, young Toomey made a sudden switch that sent him upon the high road of success in medical practice, teaching and research.

Upon his graduation from John Carroll, he considered three careers—that of a clergyman, doctor or lawyer. At that time he considered the career of medicine out of the question. It was too expensive. He had worked hard from early boyhood, earning his own way and helping earn the livelihood of his family. So he could easily visualize the

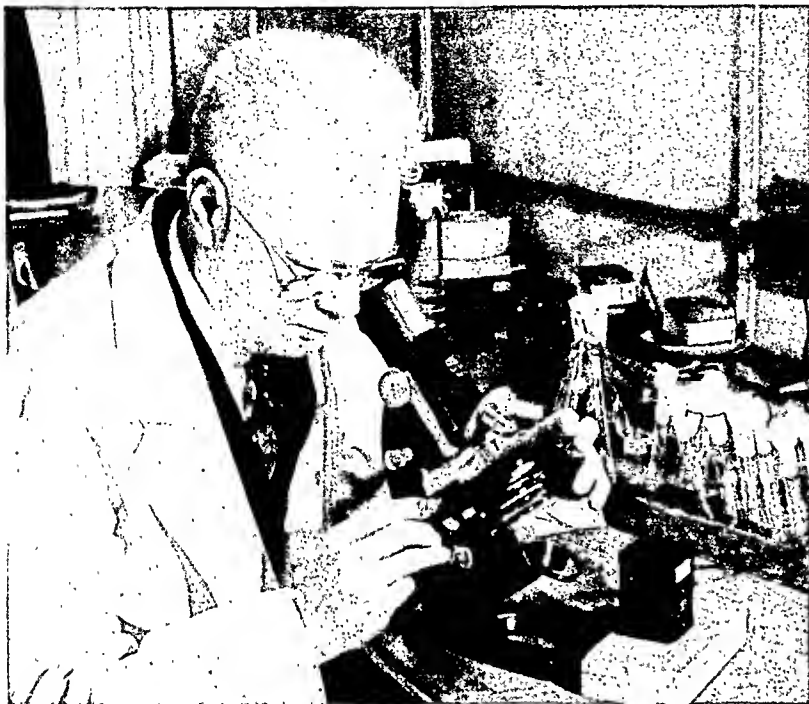
struggle he would have to undergo to earn his way through medical school. He says he was not "good enough to be a clergyman." For one thing some of his ordinary vocabulary might not sound so well from a pulpit. So he gravitated into the law, and after a good record at law school, he passed the bar examination.

Self analysis told him that the legal profession seemed best suited to his temperament. It was logical for a young man, who had learned to fight his own battles, to think he could make a living in a profession that demanded such training. He had a ready tongue. The right words flowed out easily. His speech was disarming. So law seemed to be the answer.

But he had hardly put his feet under the desk in his law office, and tacked his shingle on the office door before he became ill at ease. He felt he had made an unwise choice. Law, after all, did not seem to be the right profession.

"Our clients came in for help and advice," he relates. "Most of them were good, honest people who had made mistakes. But they had hardly stepped inside the office door before the lawyers wanted to know how large their bank accounts were or what other assets they had. That was too cold blooded for me. I got out."

He decided to go into medicine. He had worked in Cleveland hospitals to make money to pay his way through college, and the work of the doctors appealed to him. He decided to study for a medical career and enrolled at the School of Medicine at Western Reserve University. Although he worked hard in school, he was not a grind.



JOHN AUGUSTUS TOOMEY,
M. D.

he had to study he did so, and when it came time to relax he knew how to do that.

Before attending Western Reserve, "for practical monetary considerations," he took the job as assistant superintendent of Mount Sinai Hospital in Cleveland—a job that was not much to his liking. He then became steward at the Cleveland City Hospital. He did not last long as a steward, however, because—his colleagues say—he was too honest for the job. But during his stewardship the books at City Hospital ran into the black for the first time in the history of the institution. Neither the Democratic nor Republican city politicians wanted to keep him there because he failed to play the game according to their formula. He was fired from that job.

WHEN HE WAS graduated from Western Reserve's School of Medicine—at the age of 30—he knew the inner workings of hospitals well. During the first year of internship at City Hospital, which is affiliated with Western Reserve, he

was appointed medical superintendent. The contagious ward was newly created, and it became one of his charges. Treating the children brought there suffering from polio, scarlet fever, smallpox, and a long list of other contagions, he became attracted to the practice of pediatrics, and has pursued that career ever since.

Soft spoken and cheerful, Dr. Toomey has a reassuring manner that inspires confidence in the most irritable child or parent. There is no child so belligerent that he does not succumb to Dr. Toomey's gentle and good humored ways. There is no ruffled, worried or hysterical parent that he is not able to calm by his mild and disarming manner.

Commenting on his way with parents and children he says, "All that I have to do is to use a little horse sense. I try to be truthful and honest. If I find a child will not recover or its disease is fatal, I tell the parents frankly. There is no use beating around the bush about it."

He goes about City Hospital dressed in a long white gown that extends from his chin to the tops of his shoes. His office at the hospital is small with

a tiny cubicle of a waiting room, about large enough for a desk and four or five chairs. There is barely more than enough room in his office for a desk, a few bookcases filled with books, a wash basin and an elevated cot where he examines his patients. The office is comfortably cluttered with papers, hooks and a few instruments.

His manner, and his methods of handling parents and children have been profitable, not only in terms of friendship and personal satisfaction, but also in terms of money for his extensive researches. Parents have been a good source of funds.

Dr. Toomey is brusque, and his language is pungent, but he has a power and force that make people like him. Those who work for him and with him, in the hospital, and laboratory and at Western Reserve University, where he is professor of clinical pediatrics and contagious diseases, have a strong loyalty to him.

He says his hobbies are "sleeping, reading detective stories and going to Florida once a year." He does take his wife and four children to Florida and reads detective stories. But his hobbies go beyond that. It does not take too long to find out that Dr. Toomey's extra-curricular literary tastes are not confined to detective stories. When necessary he can sling out an apt quotation from Plato, Gracian, Ben Butler, Cardinal Newman, John Stewart Mill, or the Bible. And his colleagues at City Hospital say that his chief hobby is helping other people.

Men and women who have worked for him in the department of contagious diseases at City Hospital, where he is physician in charge, or in his research laboratory, have stayed with him despite many periods of low salary or uncertain pay. They know that if they come to him with a problem, whether it is moral, legal, or a difficult family or financial problem, he will employ his whole weight of intelligence, intuition, experience or judgment to help them solve it.

"We all make mistakes," he says. "But some of us are not slick enough to cover up."

Dr. Toomey may use his legal knowledge in the pursuit of his hobby of helping others, but he has never used it to enhance himself. He has never been a "chronic court testifier," as one colleague expressed it.

SINCE 1923 he has published over two hundred scientific papers on contagious diseases, anti-toxins, vaccines, immunity, serums and related subjects. He has also contributed to several medical texts.

His views on poliomyelitis and the treatment of paralysis, have, for many years, involved him in controversies with other members of the medical profession.

Receiving victims of this disease into City Hospital and watching many of them become helpless cripples, Dr. Toomey, early in his career, looked upon plaster casts for paralysis victims with a great amount of misgiving. Shortly after Dr. Toomey had entered the practice of pediatrics the late Dr. Paul Feiss, who had come to Cleveland's Mount Sinai Hospital from Harvard University, had been treating paralysis victims without the aid of casts.

"We talked and argued," Dr. Toomey relates. "He was argumentative and so was I. I couldn't go along with him fully, but he seemed to know what was fundamentally right. In 1912, while at Harvard, he was the first to impinge the nerves in their shells. When this was done, other nerves would spring forth at the point of impingement. This was the basis for the present operation of neurotrippsy.

"As a result of those conversations and arguments, I became interested in the disease. And I have never advised the use of casts." Dr. Toomey's method involves massage and almost immediate treatment of the paralysis at its earliest onset.

Students of Dr. Toomey's at Western Reserve have been amazed at his ability to detect the faintest signs of paralysis.

His ideas were revolutionary and created a great amount of antagonism toward him which has continued until the present time. In spite of the opposition—from men of a much greater amount of experience and standing—young Toomey persisted.

"Soon the public schools began to notice that they did not have so many hopeless cripples," he relates, "and gradually the method infiltrated into the consciousness of physicians."

Perhaps more stormy has been his controversy with other scientific and medical men over the por-

tal of entry of the polio virus into the human system. More than twenty years ago he purported to show that the portal of entry was not the respiratory tract. His ideas were at first rejected flatly. Then medical men began to realize that the solution of the problem of the portal of entry of the polio virus was not so simple as they formerly had thought.

Gradually more medical men have accepted his idea that portal of entry is the gastro-intestinal tract.

"I suppose I have been a problem child among medical men," he says. "I sit back and listen to a lot of bunk and never say much. I try not to interfere, but when I am asked my opinion I give it the best I can."

This is not to say that Dr. Toomey is unreceptive to ideas. Just the opposite. He says he will listen to any idea "no matter how ratty."

"Most advances in medical research come from individuals who have ratty ideas and try them out. If Banting ever had known what was in the literature, he would never have discovered insulin. Authority is the least valuable form of evidence.

"I have had so much experience in trying out ideas that I never consider an idea hopeless even though it is far fetched. I never dismiss an idea just because of some preconceived knowledge I don't believe it to be true. I believe that you should give the fellow who brought out the idea at least the benefit of some thought.

"All sorts of people come into my office, and I listen to them. I never turn them away without hearing their stories. Patients and members of patients' families have supplied me with very good suggestions. I never turn them down.

"I always like to recall that Theobald Smith made his reputation listening to cattlemen in Texas. He turned their homely observations into positive achievements.

"How can I separate the wheat from the chaff? I just use common ordinary horse sense.

"I don't like planned research, and few medical men are able to plan research anyway."

Dr. Toomey has the personality that makes a good medical research man. He combines aggressiveness, stubbornness, brusqueness and ruth-

lessness with natural intelligence. He has the courage to stand up to his adversaries with his beliefs in face of opposition that would make many others cringe and retreat. In his research he has largely worked alone, keeping as his aides loyal, hard-working, and humble men and women who swear by him and his ideas.

His students have been the beneficiaries of his years of accumulation, through reading and practical experience, of a profound philosophy of living and getting along with people. In addressing a recent Western Reserve Medical School graduating class he told the students to "be modest and not loud. Do not harangue the market place and issue a ukase on every trivial thing.

"A prudent silence is always commendable. Speak softly and in good time, and an air of wisdom may be gained. Be not always silent, though if only 'for fear that you might be reputed wise for saying nothing.'

"It is not good taste to talk about yourself. The subject never interests others. Nor should one coyly disparage his own abilities, expecting spoken refutation from the listener. He always secretly agrees with your spoken words.

"Be reserved. Keep something to yourself; don't tell all you know. People will pause longer at your word if they are not quite sure that it is all you have to say. If you've said it all, why should they wait further."

By religion a Roman Catholic, Dr. Toomey believes more in the practical application of religion than in its form, and he admits his church attendance is not too regular. He married Mary Louise Bagot, a Protestant Episcopalian, in 1918 while she was employed as a dietician at the former Thomas Normal Training School. His eldest son, Charles Hugh, is a physician, having graduated from the Western Reserve University Medical School in 1945. One daughter, Frances, was graduated from Vanderbilt University in 1944, and another is attending Flora Stone Mather College at Western Reserve University. John A. Jr., is in preparatory school in Cleveland.

A member of many medical and other scientific societies, Dr. Toomey was recently elected president-elect for 1949 of the American Academy of Pediatrics.

What Other Editors Think

Editorial Evaluations of Current Contributions To Medical Progress

CINEPLASTIC AND KRUKENBERG AMPUTATIONS

THE unused muscle bellies in amputation stumps of arm and forearm have long challenged the ingenuity of surgeons; nor has the design of upper-limb prostheses yet advanced far enough to discourage attempts to utilise the power buried in these stumps. Of the mechanical limbs devised and adopted in England and United States, those of Simpson and Hobbs, and the Norden limb which contains a free-wheeling device and may be described as a prosthesis within a prosthesis, all give a grip and a greater range of function than is possible with any single adjustable appliance, but their mechanical function is limited, and they are cosmetically crude.

The cineplastic operation owes its full development to Prof. Ferdinand Sauerbruch, who introduced the use of big, well-buried skin-tubes of local tissue. Since 1918 over 7000 cineplastic amputations have been performed at Sauerbruch's clinic at the Charité Krankenhaus in Berlin, and over 500 in the clinic of Prof. Max Lesche in Munich.

The cineplastic amputation, as done in Berlin, uses a local flap of skin, subcutaneous tissue, and deep fascia about 2 inches square to form the skin tunnel and the secondary defect is covered, not always completely, by a skin-graft. The operation is done under local anaesthesia. Professor Lesche's skin-flap is larger, perhaps 3 inches by $3\frac{1}{2}$ inches; the muscle tunnel is at least $1\frac{1}{4}$ inches in diameter and lies deep to three-quarters of the diameter of the muscle; the skin and fat tube is rotated through 90° before being passed through the muscle tunnel, so the suture line is proximal and away from the pressure of the peg; and the secondary defect is completely covered by a free graft.

A properly made skin-tube buried in the forearm muscles or in the triceps should give an excursion of 1-2 cm. to a peg about 7 mm. in diameter lying transversely in the tunnel, and should be capable of exerting a power of 15-20 lb.; when buried in the biceps or in the pectoralis major the excursion of the peg should be 5 cm. or more and the power over 40 lb. This power is used to give grip to an artificial hand. Extension of the digits can be provided by a spring device in the prosthesis or by a skin tunnel through the extensor muscles which give voluntary movement—according to the choice of the surgeon.

Cineplastic prostheses are fitted with blocking devices which allow the grip to be maintained without continuous muscular effort. Surgery of this kind requires close cooperation between surgeon and limb-maker. When properly made the cineplastic prosthesis has a fairly wide range of function.

In the Krukenberg forearm amputation, a pincers-like grip is provided by splitting the stump through the interosseous membrane between radius and ulna. At operation, the cleft between radius and ulna is usually deepened to 12 cm., or at least a third of the length of the stump, and is so cut that there is local skin to cover either the ulna or the radius; as a rule, cover for the denuded side is provided by a free graft, but Professor Herlyn at Göttingen uses a belly-arm flap and incorporates an excess of abdominal skin at the depth of the cleft to ensure that there is a fold of flap here, not a suture line. In cutting the cleft, care is taken to preserve the pronator teres, since it is the action of pronation which approximates the two limbs of the pincers. If necessary an ordinary upper-limb prosthesis can be fitted to the stump on occasion. The value of the Krukenberg amputation is limited, but it seems to be worth considering for men who have lost both upper limbs, and particularly for those who are also blind.

—*The Lancet*, Vol. 251, p. 910.

RENAL PATHOLOGY

FOR years the kidney has been the subject of considerable study both as regards its anatomical structure, its physiology and the pathological changes incident to it in disease processes.

At a recent meeting of the Physiological Society in England, Tructa, Daniel, Barclay and Franklin made a preliminary report on "Renal Pathology in the Light of Recent Neurovascular Studies." They called attention to the fact that with appropriate nerve stimulation in animals both with the abdomen unopened and in those in which the kidney had been exposed, the renal blood flow may be diverted from its commonly accepted course, and as a result the cortex of the kidney may be partly or wholly deprived of its blood supply.

In their studies they utilized roentgenographic methods and demonstrated these changes in a most striking manner. They found (as a result of the application of a tourniquet for a number of hours to the left hind leg) that the left renal circuit time was shortened by virtually a half, though the caliber of the renal artery was at the same time reduced by a quarter. The only possible explanation of these simultaneous effects was, in their opinion, a vascular short circuiting.

Further proof of this conception of short circuiting of the circulation was shown in laparotomized animals after various types of nerve stimulation. Also, they observed the blue color of the blood in the renal vein changed partially or wholly to red. In some animals the appearance of the red blood was observed to be accompanied by pulsations of arterial type. They also observed that red stream lines appeared in the renal vein after the renal cortex had paled and while it still remained pallid, and that dyes injected into the arterial side of the circulation appeared in the renal vein but did not stain the surface of the kidney, and on section the cortex was seen to be unstained while the medulla, and especially its subcortical part, was deeply colored by the dye.

These observations made on the left kidney were in marked contrast to the right unstimulated kidney in which both cortex and medulla were stained. The former, namely the cortex, was more deeply stained than the medulla. These observations made

with the use of dyes were confirmed by roentgenographic methods.

The investigators concluded that as a result of appropriate nerve stimulation the blood supply may be diverted wholly or partly from the cortex and short circuited through medullary (especially subcortical) blood channels. The large potential capacity of these by-passing channels enables them to transmit the whole of the renal blood inflow whenever the supply to the cortex is diverted and the latter thereby rendered ischemic.

Also it seems probable and most likely that nerve stimulation could be produced centrally or peripherally by a variety of noxious agents and that the picture seen in many loosely related syndromes is the result of a defense device by which the cortex of the kidney is excluded from the circulating toxin or other noxious agent, and thus protected.

These observers think that this same protective mechanism may fulfill another role in hemorrhage and shock or conditions with decreased blood volume by preventing the blood from reaching the filter of the kidney, namely the cortex, and thus conserving fluid.

These fundamental experiments may and probably will lead to an elucidation of a host of diseases in which the kidneys play an important part.

The American Journal of Roentgenology and Radium Therapy, Vol. 57, p. 252.

PSYCHONEUROSIS

PSYCHOGENIC diseases are in the limelight today. The problems they created in the induction centers and later in the armed forces aroused and demanded justifiable attention. Their importance in civilian life is no less urgent. Although better understood now than in the past, there is yet much to be explained.

The psychiatrists and psychologists, not without exceptions, have stressed the psychologic aspects almost to the exclusion of the physical phase in consideration of etiology whereas other large groups of clinicians have been so fascinated with the findings of purely pathologic lesions as to ignore any other explanations for any bodily complaints. These opinions, are now being challenged

by many internists and other investigators who believe that practically all diseases have really two components, namely, the mental and the physical. They argue that any condition which affects the body will also involve the mind and vice-versa to a certain intent. This concept is considered to be particularly pertinent in the large group usually classified as the psychoneurotic or psychogenic. They contend that only with a proper evaluation of these two factors will a proper understanding of these disorders be made and any rational attempt at treatment be secured.

Recent physiologic studies have helped substantiate these ideas. It is known that conditions such as emotional disturbances affect the autonomic nervous system resulting in visceral changes in the cardiovascular, gastro-intestinal, respiratory or other systems of the body.

Various problems relating to the symptoms have been studied and information from different sources has been made available to show definite physiologic changes. Wolf has demonstrated by actual measurements how anxiety, anger and tension lead to inefficient pulmonary ventilation causing dyspnea. The effect of similar emotional stress and strain on blood pressure or coronary vessels producing heart pain has been substantiated. Anxiety states have been reported by Sargent, to be a factor in the production of actual muscular tension and even fibrillary twitchings in a group of soldiers hospitalized for backache. The sugar tolerance curves have been found to be abnormal more frequently in patients with a diagnosis of psychoneurosis than in controls. The results of other experiments along those lines have appeared recently.

Archives of Physical Medicine, Vol. 28, p. 237.

BACITRACIN

NEW and effective antibiotics are being discovered from time to time. Some of these antibiotics are very limited in their field of service, others show remarkable effect on many organisms.

One of the latest, apparently very effective of

these antibodies was reported on by Johnson, Anker and Meleney in *Science* this fall. This report aroused a great deal of enthusiasm and there are numerous investigators who are anxious to obtain the material to study its effect in various types of infection. Meleney and Johnson have now reported on the first hundred cases of surgical infections treated locally with this particular medicament.

Bacitracin is a filtrate of an aerobic gram-positive, spore-forming bacillus which has a wide field of antibacterial activity. The preparation has gradually been refined and with this refinement necessarily it has been possible to reduce the size of the dose.

In this present report the drug was used entirely locally, injected directly into furuncles and boils and into deep and superficial abscesses, or applied topically, as in a sty or ulcer of the leg. The cases were not selected and represent the average run of infection which is observed in an ambulatory clinic.

Meleney and his associate found that in 31 cases the results of treatment were excellent, in 57 good, in nine questionable and in only three was there no effect. Bacitracin was found effective in most infections which are resistant to penicillin and in some that did not respond to this particular antibiotic and in only a few instances in which bacitracin failed to bring about a cure did the subsequent response to penicillin become effective.

The medicament is given in two forms; an aqueous solution and the other a water soluble ointment. The aqueous solution was injected directly into the lesion, the ointment was used in such sites where occurred ulcers or directly in the eye in the instance of styes and conjunctivitis.

The authors point out that this new antibiotic which is not locally toxic or irritating and is not inhibited by blood or pus, will be of clinical importance if it can succeed where penicillin or the sulfonamides have failed. Their observations, moreover, point out that this preparation is active against many organisms, coccal in nature, which are resistant to the other two important medicaments.

New Orleans Medical & Surgical Journal, Vol. 99, p. 523. John H. Musser, M.D., Editor in Chief.

Consultation Service

We offer this special consultation information service as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from members of our editorial board best qualified to help. Each question will be answered by mail and answers of general interest will be published each month.

BLOOD PRESSURE VARIATION

QUESTION: Could you tell me if there is any significance in the fact that a patient has a marked discrepancy in the blood pressure in either arm? She has a BP 136/80 in the left arm and BP of 170/100 in the right arm. Her weight is 212 pounds and she is 46 years of age.

M. D.—Minnesota.

ANSWER: A discrepancy in the blood pressure in the arms may occur with the scalenus anticus syndrome cervical rib aortic aneurism, and occlusion of the brachial axillary or subclavian arteries.

A variation of 10 to 15 mm. in the blood pressure in the arms may occur normally in some individuals as a result of an anatomical difference in the placement of the vessels.

FALSE SUGAR REACTIONS

QUESTION: What drugs tend to cause false reactions in testing for sugar? What amount of aspirin will cause such an error?

M. D.—North Dakota

ANSWER: The following drugs have been known to cause in concentrated urine an atypical reduction of some of the copper solutions, chiefly Fehling's Solution: Cincophen, Neo-cincophen, salicylates, amidopyrine; also some of the conjugated glycuronic acids decomposing in the urine

after the ingestion of chloral hydrate, camphor, menthol, turpentine or phenol. It might also be stated that excessive amounts of creatinine, uric acid, and chloroform will reduce some of the copper solutions.

However, if one is experienced in doing urines, the reaction will frequently be found to be atypical. It will require at least 30 grains of aspirin to be taken three times a day for this amount to give a reduction of Fehling's Solution, although individuals differ greatly in this respect.

TRICHOMONA URETHRITIS AND PROSTATITIS

QUESTION: A white man, age 37, has complained of a urethral discharge of three months' duration. Various smears were apparently negative for gonococci. He has received both sulfonamide and penicillin therapy from other physicians. I do not know in what amount this therapy was given. When the patient was first seen, a few trichomonads were found in his urine specimen and the urethral smear showed mixed gram positive and negative cocci and a few gram negative bacilli. He has improved somewhat on rather large doses of atabrine, given during the past two weeks, and penicillin has cleared his secondary infection. However, he still has a few trichomonads in his prostatic secretion. What is the accepted treatment of trichomonas urethritis and prostatitis?

M. D.—Iowa

ANSWER: Pyridium by mouth has been useful. Massage of prostate gland and instillation of 0.5 per cent to 2 per cent aqueous mercurochrome solution into bladder neck, prostatic urethra and pendulous urethra. The arsphenamines may be given by vein in moderate size doses. Treat wife or sexual partner.

New Drugs

The information in this department has been supplied to *Postgraduate Medicine* by the manufacturers of the products described.

QUATRESIN 1:1,000, SOLUTION

PURPOSE: Germicide.
COMPOSITION: Myristyl-gamma-picolinium chloride—0.1 per cent.
DESCRIPTION: A highly potent and non-irritating surgical germicide in aqueous solution. To be used in disinfecting the skin and mucous membranes, irrigation of deep wounds, sinus tracts, compound fractures, or bladder, or urethral irrigations.
ADMINISTRATION: Apply undiluted or diluted up to 1:10.
HOW SUPPLIED AND PRICE: Pint. \$0.70; gallon. \$4.60.
PRODUCER: The Upjohn Company, Kalamazoo 99, Mich.

QUATRESIN 1:500, TINCTURE

PURPOSE: Germicide.
COMPOSITION: Myristyl-gamma-picolinium chloride—0.2 per cent.
 Acetone—10.0 per cent.
 Alcohol—50.0 per cent.
DESCRIPTION: Highly potent surgical germicide in alcohol, acetone, aqueous solution. For use in skin and mucous membrane disinfection and first aid antiseptics.
ADMINISTRATION: Apply undiluted or diluted up to 1:10.
HOW SUPPLIED AND PRICE: Pint. \$0.90; gallon. \$5.75.
PRODUCER: The Upjohn Company, Kalamazoo 99, Mich.

"TABLOID" PENICILLIN CALCIUM (BUFFERED) 50,000 UNITS

PURPOSE: In the prevention of secondary infections.
DESCRIPTION: A new oral product, buffered with sodium citrate.
INDICATIONS FOR USE: "Tabloid" Penicillin Calcium is indicated in the prevention of secondary infections such as those following tonsillectomy, tooth extractions and similar conditions. It is used in conjunction with parenteral therapy in gonorrhea, pneumococci, staphylococci and streptococci infections.
HOW SUPPLIED: Sealed in foil strips and supplied in boxes of 20.
PRICE: \$7.00, list.
PRODUCER: Burroughs Wellcome & Co., New York, N. Y.

MEPRANE

PURPOSE: For prompt relief of menopausal symptoms without unpleasant side reactions.
COMPOSITION: Each tablet contains 1 mg. (1/65 grain) 3, 4-bis- (m-methyl-p-propionyphenyl) hexane.
DESCRIPTION: A non-steroid compound, strongly estrogenic, and exceptionally well tolerated. Colorless crystals or a white microcrystalline powder. M.P. 113 to 115° C.; odorless; readily soluble in ether, acetone, and ethyl acetate; slightly soluble in alcohol; insoluble in water, dilute acids and dilute alkalies.
INDICATIONS FOR USE: In the clinical manifestations of hypoestrinism as in the treatment of menopausal symptoms. It is indicated for the suppression of lactation.
DOSEAGE: Menopause: Initial therapy—1 Meprane tablet i.d.; maintenance therapy—1 to 2 tablets daily. For the suppression of lactation: 1 tablet q.i.d. for three days. Dosage in other conditions on request.
CAUTIONS: Those that generally apply to natural and synthetic estrogens.
HOW SUPPLIED: In packages of 30 and 100 individually wrapped tablets. Each tablet contains 1 mg. Meprane.
PRICE: Package of 30s. \$7.80, doz.; \$0.65 each
 Package of 100s. 19.80, doz.; 1.65 each
PRODUCER: Reed and Carnrick, Jersey City 6, N. J.

PUROGENATED TOXOIDS

Purogenated Diphtheria Toxoid, Alum Precipitated; Purogenated Tetanus Toxoid, Fluid; Purogenated Tetanus Toxoid, Alum Precipitated; and Purogenated Diphtheria-Tetanus Toxoid, Alum Precipitated.
PURPOSE: Elimination of unpleasant local and constitutional reactions following immunization against diphtheria and tetanus.
COMPOSITION: Proteins, sorted out by fractionating a solution of mixed proteins with wood alcohol at low temperatures.
DESCRIPTION: The new toxoids are 99.7 per cent nitrogen-free, the nonantigenic nitrogen having been reduced to 0.15 per cent approximately. In the forms alum-precipitated, the alum content has been reduced by 75 per cent.
DOSEAGE: Dosage required is only one-half the volume usually needed with standard toxoids.
PRODUCER: Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

After Hours

CLEVELAND'S HOBBYISTS

Probably the number of physicians whose hobbies have been discovered is no greater in Cleveland, Ohio, than in other large cities. However this month we are directing our attention to some of the Cleveland doctors and their avocations.

* * *

THE LITERARY GROUP

A man who has always taken keen delight in pleasurable and interesting hobbies is Dr. William T. Corlett, who at age 92, is only in the afternoon of his busy life. Doctor Corlett, long a practitioner of dermatology and syphilology, is now retired. He continues to be active by writing and publishing, at regular intervals, a book of poetry, memoirs or history. It is an inspiration to watch his enthusiasm and accomplishment.

The Cleveland Medical Library has several rooms furnished and endowed by gifts and bequests of members. Among these is the Corlett room endowed by Doctor Corlett, Professor Emeritus of Dermatology, Western Reserve University. The room is set apart for the study of dermatology and is adorned with portraits, busts, prints and photographs of those who contributed to this phase of medicine. The room reflects, to a certain degree, the life work of its donor, containing as it does his library and the furnishings used by him during his long period as a practitioner.

A few years ago Charles C

Thomas published Doctor Corlett's "The Medicine-Man of the American Indian and his Cultural Background," a medical picture of most of the aboriginal tribes of the Americas. Doctor Corlett hopes others will study this subject before the old people of the tribes die. Because the offices of priest and physician are combined as one in the medicine-man of the American Indian, the book treats of religion as well as medicine and is almost as much concerned with theology as with pathology.

* * *

A PSYCHIATRIST'S HOBBIES

The Cleveland Literary group also includes Dr. Louis J. Karnosh, whose book, "A Psychiatrist's Anthology," offers three little poetic gems — "Melancholia," "General Paresis," and "Paranoia." In addition to his literary proclivity, Doctor Karnosh has produced some outstanding wood carvings. One specimen was a nationally advertised radio cabinet. Oil painting and fine printing are his other hobbies.

* * *

OUTDOOR PURSUITS

During extended visits about southern waters, Dr. R. E. Barney has accumulated a valuable collection of shells. Dr. William H. Weir has had great enjoyment in his



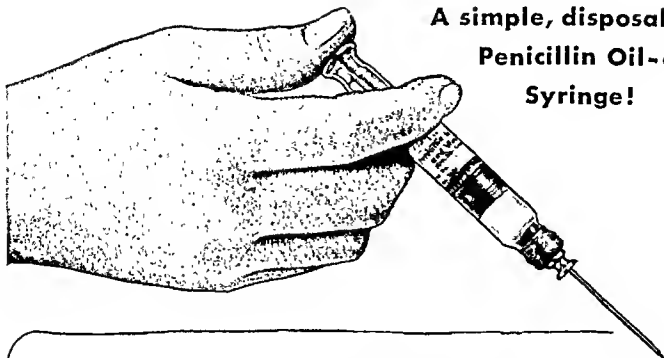
Dr. Norman C. Yarian examines some flasks of orchid seedlings which are being grown upon culture media.

garden, being particularly successful with daffodils. "While I can't give much time to the breeding of new varieties," says Doctor Weir, "I am a real daffodil enthusiast and my blooms make a fine showing."

Dr. E. P. McCullagh and Dr. N. C. Yarian have pursued their quests widely, the former for birds' eggs and the latter for orchids. Doctor Yarian has, for the past 18 years, given considerable attention to the study, culture and photographing of orchids, collecting specimens from Central America and Mexico. He writes for various journals on orquidea and is often asked to speak about orchids.

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If your pharmacist hasn't these easy, disposable syringes in stock now—ask him to order you a supply to save time and nuisance in your practice.

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Notes On Contributors

DANIEL C. ELKIN, M.D., received his A. B. degree from Yale University and the M. D. from Emory University in Atlanta, Georgia. In 1940 Dr. Elkin was awarded the Matas medal for vascular surgery from Tulane University and in 1945 he was honored with the Legion of Merit. He is the author of "Medical Reports of John Y. Bassett." Dr. Elkin is a Fellow of the American College of Surgeons, and a member of the American Association for Thoracic Surgery, American Medical Association, American Surgical Association, The Society of Clinical Surgery and the Southern Surgical Association.

MAXWELL HARBIN, M.D., graduated from the University of Georgia with the B.S. degree (1916) and received the M.D. degree from Harvard Medical School (1920). He is associate clinical professor of orthopedic surgery at Western Reserve University Medical School and chief of the Division of Orthopedic Surgery of the University Hospitals in Cleveland. Dr. Harbin is a member of the American Academy of Orthopedic Surgeons, Eastern Surgical Society, Central Surgical Society and the American Medical Association.

THOMAS E. JONES, M.D., graduated from Western Reserve University with the A.B. degree in 1913 and the M.D. in 1916. Dr. Jones is a member of the American Surgical Association, Central Surgical Association and a Fellow of the American College of Surgeons.

DREW LUTEN, M.D., associate professor of clinical medicine at Washington University in St. Louis, attended the University of Kentucky from which he received the A.B. degree and was granted the M.D. degree from Johns Hopkins. Dr. Luten is the author of "The Clinical Use of Digitalis." He is

a member of the American Heart Association, the Central Society for Clinical Research and the American Medical Association.

RAYMOND C. MCKAY, M. D., is a graduate of Brown University (A.B.) and of the School of Medicine of Western Reserve University where he received the M. D. degree. Dr. McKay is associate clinical professor of Medicine at Western Reserve University, Medical Director of the Tuberculosis Department of the Cleveland City Hospital, and is a member of the Board of Silicosis Referees of the Ohio State Industrial Commission. He is a member of the American Trudeau Society, the American College of Chest Physicians and the American Medical Association.

WALTMAN, WALTERS, M.D., completed his undergraduate work at Dartmouth College where he received the B.S. degree. He graduated with the M.D. from Rush Medical College and holds the degree of M.S. in surgery from the University of Minnesota, the honorary degrees of D.Sc. from Dartmouth and LL.D. from Hahnemann Medical College. Dr. Walters was awarded the gold medal for a scientific exhibit by the American Medical Association of 1941. He is the author of the following book sections: "Carcinoma of the Stomach" by H. K. Gray and J. T. Priestly; "Gall Bladder and Bile Ducts" by Albert M. Snell; "Surgery of the Pancreas" in the "Cyclopedia of Medicine" by G. M. Piersol; "Total Gastrectomy for Carcinoma of the Stomach" in "The Stomach and Duodenum," by G. B. Eusterman, D. C. Balfour and members of the staff of the Mayo Clinic and Mayo Foundation; "Stricture of the Bile Ducts" in "A Textbook of Surgery" by Frederick Christopher; "Surgery of the Biliary System" in "Practice of Surgery" by Dean Lewis, and is chief editor of "Lewis Practice of Surgery." Dr. Walters also serves as chairman of the editorial board of the *Archives of Surgery*.

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American	\$2.50-\$3.50	\$3.50-\$4.00	\$4.00	\$6.00
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Claridge	3.00- 4.00	4.00- 6.50	5.00- 6.50	10.00 & up
Coronado	3.50- 6.00	5.25-10.00	5.50-11.00	8.50- 15.00
DeSoto	2.75- 7.00	4.00- 7.00	6.00-12.00	10.50- 12.00
*Jefferson	3.50- 6.00	5.00- 7.00	7.00- 8.00	14.00- 22.00
Kingsway	3.20- 3.80	4.80- 5.30	5.80	8.50
Lennox	3.25- 6.00	5.00- 6.50	6.00- 8.00	11.00
Lindell Plaza	2.50- 3.00	3.00- 4.00		
Majestic	2.25- 3.50	3.00- 4.00	5.00	
Mark Twain	3.00- 3.50	4.50- 5.00	5.00- 5.50	
Mayfair	3.25- 7.00	4.50- 8.00	6.00- 8.00	11.00 & up
Melbourne	3.50- 6.00	5.50- 6.50	6.00- 8.50	12.00- 15.50
Park Plaza	4.00- 8.00		5.50-10.00	10.00- 15.00
Roosevelt	3.00	3.50- 4.50	4.50- 6.00	15.00- 26.00
*Statler	3.50- 6.00	5.25- 8.00	7.25-10.00	16.00- 19.00
Warwick	2.25- 3.50	3.25- 5.00	5.00- 6.00	

Apply early. All reservations must be received by September 29, 1947.

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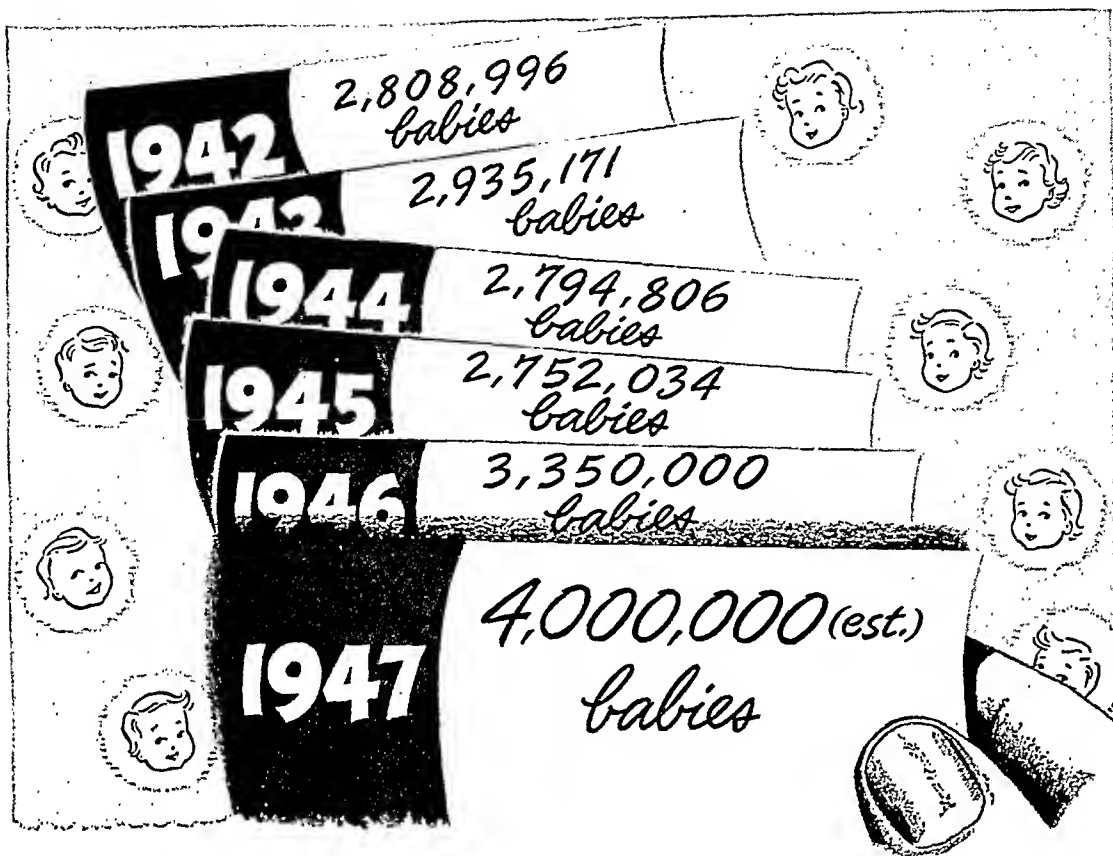
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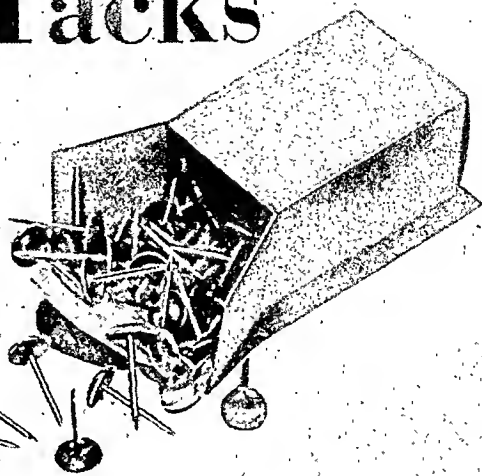
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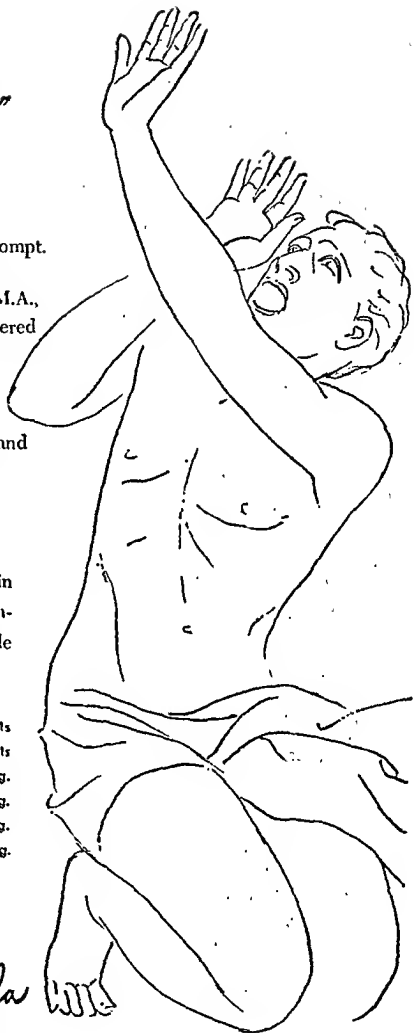
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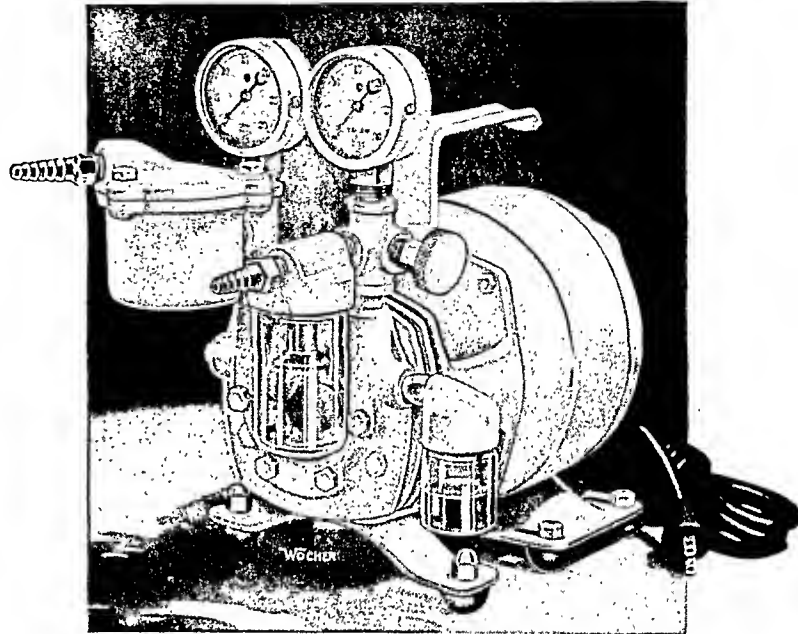


1. Peters, J. P., and Elman, R.: J.A.M.A. 124:1206 (Apr. 22) 1944.
2. Council on Foods and Nutrition: J.A.M.A. 131:666 (June 22) 1946.

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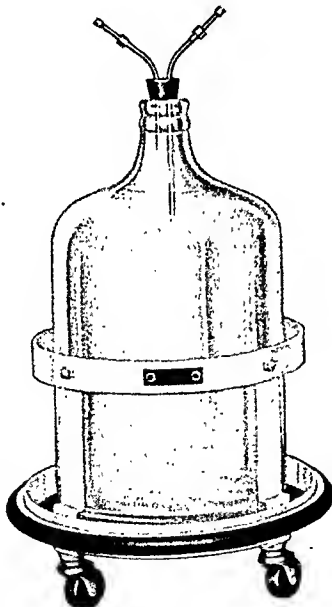
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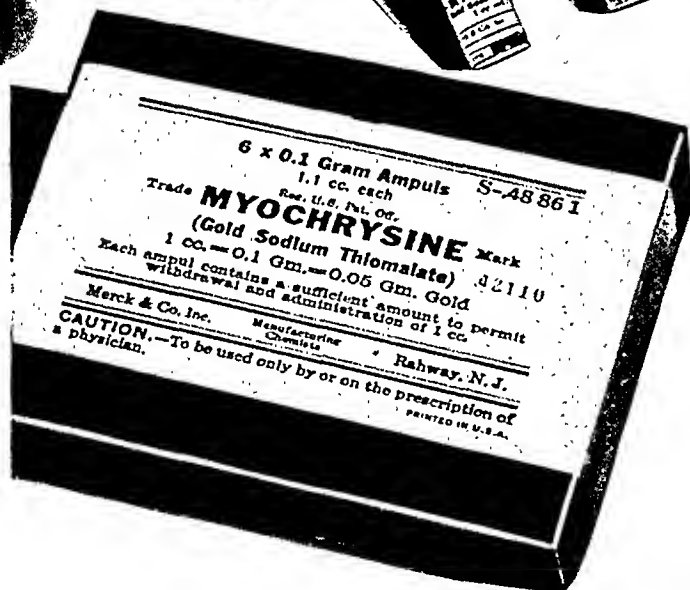
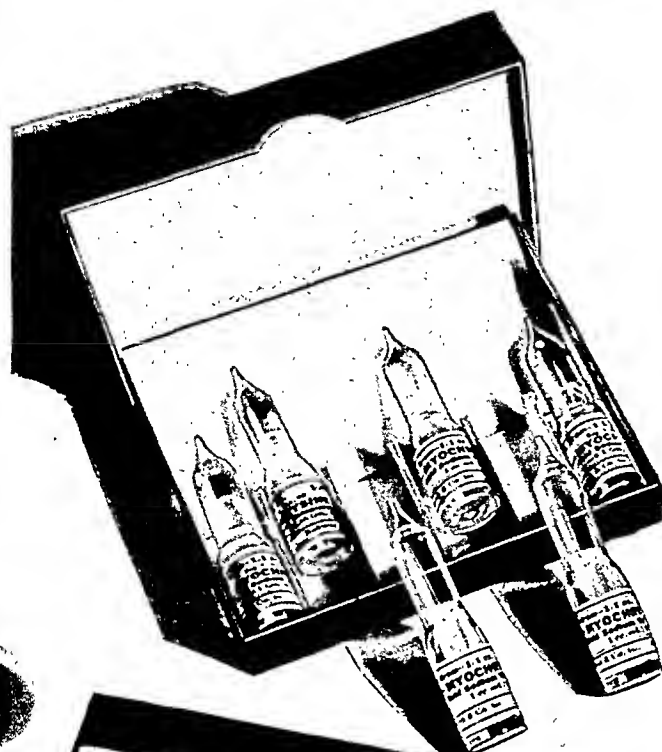
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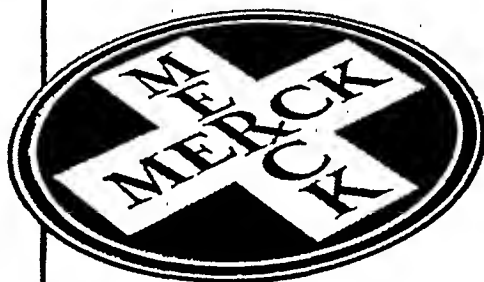
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¹Barrett, L., Brit. M. J., 1:601, 1942; ²Serravallo, E. L. and Fabbiani, G. E., Ann. J. Med. (Vol. 13, March, 1947); ³Finley, R. S. and Barker, S. I. J.N.W.A., 13:56, 1946; ⁴Finley, R. S. and Barker, S. I., A Preliminary Evaluation of Dienestrol in the Menopause, Am. J. Obst. and Gynec. (Vol. 53, March, 1947); ⁵Compton, A., Rabin, A. E., et al: Preliminary Studies of Dienestrol (Trade Name) to be published; ⁶Chadon, E. S.: Value of Dienestrol in the Menopausal Syndrome (Abstracts) to be published.

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VOLUME I, Number 2

FEBRUARY 1947

Special articles in this issue

TREATMENT OF SURGICAL INFECTIONS BY CHEMICAL AND ANTIBIOTIC AGENTS

Frank L. Meleney, M. D., ASSOCIATE
PROFESSOR OF CLINICAL SURGERY, COLUMBIA
UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS

SEROLOGY AND OBSTETRICS

Rae T. LaVake, M. D., CLINICAL ASSISTANT
PROFESSOR OF OBSTETRICS AND GYNECOLOGY,
UNIVERSITY OF MINNESOTA MEDICAL SCHOOL

TREATMENT OF DIABETIC ACIDOSIS AND DIABETIC COMA

Edvard Tolstoi, M. D., ASSISTANT
PROFESSOR OF CLINICAL MEDICINE, CORNELL
UNIVERSITY SCHOOL OF MEDICINE

Diagnostic Clinics

THIOURACIL, THIOBANTHAL, PROPYL THIOURACIL -
the TREATMENT of HYPERTHYROIDISM

Frank H. Lahey, M. D., DIRECTOR
LAHEY CLINIC, BOSTON, MASS.

TREATMENT OF PERNICIOUS ANEMIA

Russell L. Haden, M. D.

DIFFERENTIAL DIAGNOSIS OF
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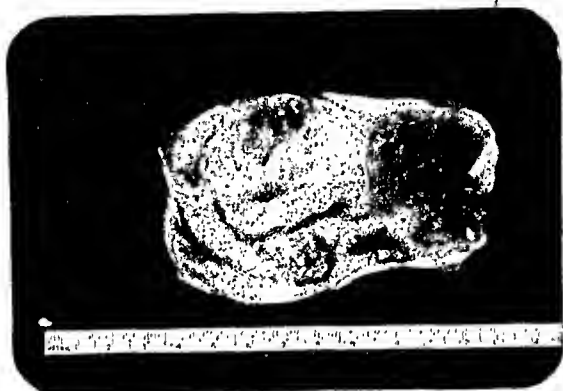
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1. Rehfuess, M. E. *Indigestion: Its Diagnosis and Treatment*, Philadelphia, W. B. Saunders Company, 1943, pp. 278, 336.

2. Dolkart, E. E.; Jones, K. K., and Brown, C. F. *Can. Arch. Int. Med.* 62:418 (Oct) 1938.

3. Annegers, J. H.; Snape, F. E.; Ivy, A. C., and Atkinson, A. Jr. *J. Lab. & Clin. Med.* 29:553 (Aug) 1944.

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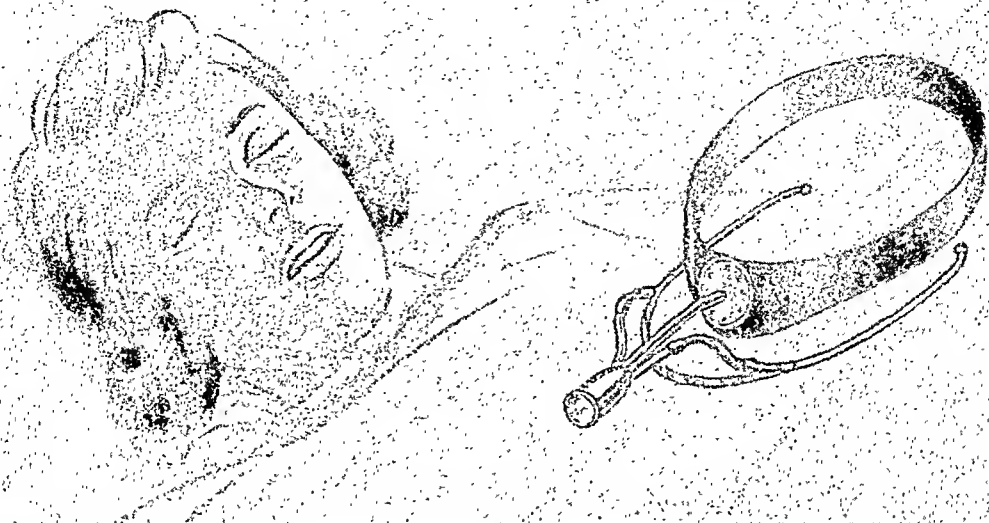
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FEBRUARY, 1947

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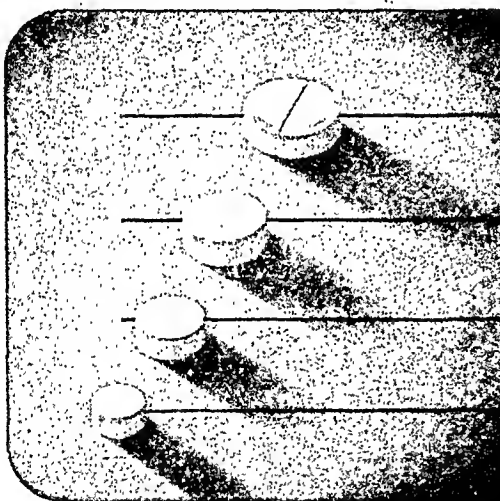
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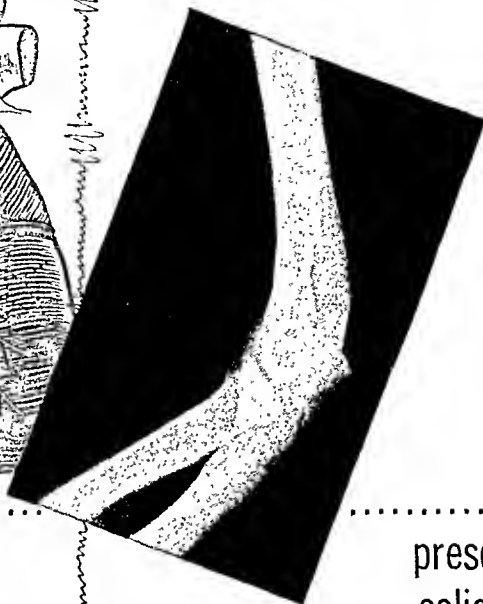
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(1) Link, K. P. and co-workers: Hypoprothrombinemia in the Rat Induced by Salicylic Acid, J. Biol. Chem., 147:463-474 (Feb.) 1943.

(2) Meyer, O. O., and Howard, B.: Production of Hypoprothrombinemia and Hypocoagulability of the Blood with Salicylates, Proc. Soc. Exper. Biol. Med., 53:234-237 (June) 1943.

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LAKE SIDE

Treatment of Surgical Infections by Chemical and Antibiotic Agents

FRANK L. MELENEY*

COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK

IN THE last five years an overwhelming amount of literature has appeared on the subject of infections, particularly with respect to the chemotherapeutic and antibiotic agents.

Unquestionably in the last five years these newer agents have changed the whole aspect of infection, both medical and surgical. We have to get experience all over again on the behavior of infection under treatment with these new drugs. There is a temptation to use them promiscuously, and yet certainly if we are to improve our results we must use them with discrimination.

In reality, chemotherapy is older than medical history. This we know from the old papyri found in the ancient tombs of Egypt. We know that the same infectious diseases existed in those days that we see today, and we know from the prescriptions that were written that the doctors of those times used medicaments which we now call chemotherapeutic agents.

The antibiotics, however, open up an entirely

new era, and we are just beginning to break the ground in that very fertile field.

With regard to chemotherapy, of which I should like to speak briefly at first, I wish to emphasize the point that back in the 1880's, when infectious diseases were definitely proved to be due to specific organisms, Koch, von Bering, Pasteur, and others studied the behavior and the nature of these organisms. At that time, the specific therapy of infectious diseases originated, but Koch and von Bering were par-

*Associate Professor of Clinical Surgery, Columbia University College of Physicians and Surgeons.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University College of Physicians and Surgeons, and since January 1, 1946 under a contract between the Office of the Surgeon General, U. S. Army, and Columbia University.

Read before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio, October 15 to 18, 1946.



Frank L. Meleney

Table I
SHOWING THE OVER-ALL RESULTS OF PENICILLIN TREATMENT IN SURGICAL INFECTIONS

Total Number of Cases 744	Results in Percentage					Unfavorable	
	Favorable			Question- able 17.8		No Effect 17.6	Combined 35.4
	Excellent 14.8	Good 49.9	Combined 64.7				

ticularly discouraged in trying to find an agent which would kill bacteria without injuring the host. In fact, they predicted that it could not be done, but Ehrlich continued his researches and finally was rewarded, with the aid of Browning and others, by the discovery of salvarsan. But for the diseases caused by the lower bacteria, they found no agent which did not either damage the body or become inactivated by the tissues and fluids of the body.

of these agents without a knowledge of the bacterial causes in many cases followed this discovery. I am sure that you have heard doctors say, "I didn't know what the patient had so I gave him sulfanilamide." It was given for fevers of unknown origin with the hope that it would, and in many cases it did, control the infection. But results were disappointing in many cases and time was lost because the causative organism was not known.

Table II
SHOWING THE MOST FAVORABLE RESULTS OF PENICILLIN TREATMENT ACCORDING TO DIAGNOSIS

Diagnosis	Total Cases	Results in Percentage					Unfavorable	
		Favorable-			Question- able		No Effect	Combined
		Excellent	Good	Combined				
Furuncle	26	53.9	38.4	92.3	7.7	0	7.7	
Cellulitis	36	64.0	27.7	91.7	8.3	0	8.3	
Mastoiditis	6	0	83.3	83.3	0	16.7	16.7	
Carbuncle	28	39.3	42.9	82.2	14.3	3.6	17.9	
Suppurative arthritis	22	18.2	63.5	81.7	4.5	13.6	18.1	
Lung abscess	11	0	81.7	81.7	0	18.3	18.3	
Superficial abscess	32	25.0	56.3	81.3	6.3	12.5	18.8	
Brain abscess	5	0	80.0	80.0	0	20.0	20.0	
Osteomyelitis	153	8.5	68.0	76.5	13.7	9.8	23.5	

Then came the dyes. Out of the great number of dyes tried, three gave encouraging results: gentian violet, acriflavine, and mercurochrome; but the damage which they did outweighed the benefit that they produced, and they fell into disrepute. A few research workers, however, continued the study of dyes, and out of it came Domagk's work and the demonstration that sulfanilamide, which was the active principle of his prontosil, could cure hemolytic streptococcus infections in animals. This was promptly followed by Colebrook's studies with puerperal fever, in which he clearly demonstrated that the mortality and morbidity of that common disease could be cut down by the clinical use of sulfanilamide.

I do not wish to go into the details, all of which I think are clearly in your minds, but I want to point out that the indiscriminate use

ONE thing I want to emphasize is the necessity for a clear knowledge of the etiological agent, if it be possible, in any given case, so that the proper method and agent can be used in combating the infection. I will discuss that a little later.

The limitations of sulfanilamide, particularly in pneumococcus and staphylococcus infections, led to the development of derivatives which partially met those limitations. I think that we are all convinced from our experiences that sulfanilamide took the terror out of hemolytic streptococcus septicemia. In fact, in my own hospital in New York it practically disappeared from the wards, at least from the surgical side. Occasionally overwhelming hemolytic streptococcus septicemias would come into the medical wards, but we rarely saw them on the surgical side because the initial stages of the

disease were curtailed by the use of sulfanilamide and septicemia was prevented. But staphylococcus septicemia came along in just about the same frequency, and although it was hoped that sulfathiazole might meet that situation, it failed to do so.

The use of bacteriophage was of definite benefit in staphylococcal septicemia, but the difficulty of preparing a potent bacteriophage was so great that the commercial companies putting out bacteriophage without the necessary safeguards brought it into disrepute. It failed to measure up to expectations.

ment of Agriculture, the National Research Council, the Committee on Medical Research of the Office of Scientific Research and Development, with, of course, the help of those who came from England, led to its rapid production and made it available when our armies went across the Channel.

STILL the value of these chemotherapeutic and antibiotic agents during the war has come up for questioning, and I think the consensus is that we must give credit to the splendid organization of the medical department that

Table III

SHOWING THE INTERMEDIATE RESULTS OF PENICILLIN TREATMENT ACCORDING TO DIAGNOSIS

Diagnosis	Total Cases	Favorable Results in Percentage			Unfavorable	
		Excellent	Good	Combined	Questionable	No Effect Combined
Deep abscess	58	15.5	53.4	68.9	22.4	8.6 31.0
Thrombophlebitis	12	8.3	58.4	66.7	16.7	16.7 33.4
Sinusitis	6	0	66.7	66.7	0	33.3 33.3
Infected soft-part wound	37	13.5	51.3	64.8	21.6	13.5 35.1
Infected operative wound	70	5.7	55.6	61.3	21.4	17.2 38.6
Otitis media	7	28.6	28.6	57.2	14.3	28.6 42.9
Infected compound fracture	9	0	55.6	55.6	11.1	33.3 44.4
Ulcer of the skin	22	0	50.0	50.0	18.2	31.8 50.0

Table IV

SHOWING THE LEAST FAVORABLE RESULTS OF PENICILLIN TREATMENT ACCORDING TO DIAGNOSIS

Diagnosis	Total Cases	Favorable Results in Percentage			Unfavorable	
		Excellent	Good	Combined	Questionable	No Effect Combined
Empyema	34	0	47.0	47.0	26.5	26.5 53.0
Infected burn	31	3.2	42.0	45.2	29.0	24.8 54.8
Gas gangrene	9	11.1	33.3	44.4	33.3	22.2 55.5
Actinomycosis	7	0	42.9	42.9	28.6	28.6 57.2
Gangrene of skin	10	10.0	30.0	40.0	50.0	10.0 60.0
Miscellaneous	66	13.6	25.8	39.4	16.7	43.9 60.6
Postop. pneumonia	18	11.1	27.8	38.9	38.9	22.2 61.1
Peritoneal abscess	11	9.1	27.3	36.4	45.5	18.2 63.7
Diffuse peritonitis	18	5.5	22.2	27.7	22.2	50.0 72.2

When the war began, it was hoped that the sulfonamides (by that time sulfadiazine was available) would prevent or minimize the development of infection in war wounds, but it was the limitation of these drugs in these casualties, recognized first in England, that led to the further development of other agents, and revived interest in the antibiotic penicillin, which had been discovered some years before.

I think that we should recognize that the cooperative effort made in the development of penicillin was one of the great masterpieces of the supportive medical services of the war. The cooperation of the manufacturers, the Depart-

brought good surgeons up to the front line and effected rapid evacuation of the wounded, for the low mortality among the wounded in the war, rather than to the antibacterial agents, which must be regarded chiefly as adjuncts and secondary factors.

What I have just said applies particularly to the prophylaxis of infection, but we have, of course, the equally important problem of the treatment of established infection which I want to bring out in my next remarks. Let me point out first of all the difficulty of evaluating drugs or medical adjuncts in the treatment of surgical infections. We noticed in the early days of the

Table V
SHOWING THE RESULTS IN THE THREE GROUPS REPRESENTING THE LOCAL, GENERAL, AND COMBINED METHOD OF GIVING PENICILLIN

Method of Penicillin Administration	Total Cases	Results in Percentage					
		Favorable			Unfavorable		
		Excellent	Good	Combined	Questionable	No Effect	Combined
General, without local	438	16.7	44.7	61.4	20.0	18.5	38.5
Local, without general	142	16.2	54.2	70.4	15.5	14.1	29.6
Both general and local	164	8.5	59.8	68.3	13.4	18.3	31.7

sulfonamides that on the surgical services of the hospital, our results were not as favorable as those obtained on the medical side. We asked ourselves why that was so. It is obvious that surgical infections differ fundamentally from medical infections in several important respects. Surgical infections are distinguished by being amenable to surgery, that is, to an operative procedure. Obviously, the ideal treatment of infection is its complete eradication from the body, which can sometimes be obtained by complete excision. If that cannot be done without injuring the body permanently, an incision is used as a compromise. This carries away destroyed tissue and exudate, and permits an increased circulation to the part, thus aiding evacuation of the destroyed tissue by the body.

IN THE periphery of any surgical lesion where there has been a destruction of tissue or collection of purulent exudate, there are thrombosed blood vessels which prevent any agent in the blood from penetrating into the areas where the bacteria are most active. In medical infections there is a diffuse cellulitis which permits the blood vessels to carry in the medication.

Where there is no destruction of tissue that agent can most effectively act upon the causative bacteria. Surgical infections in their initial stages are in that state, a diffuse cellulitis without a breakdown of tissue, and therefore, in the early stages these agents are much more likely to be effective.

There are certain conditions in which we know from experience that surgery has been absolutely necessary to cure the infection. Perhaps the best example of such a condition is acute osteomyelitis. It comes to us in the stage of septicemia in a very sick patient with high fever, often with chills, a positive blood culture, sometimes no local signs in any bone, but usually with some indication that the focus of infection is in the bone or near a joint. The roentgenogram does not reveal the destruction of tissue at first, but in the course of time there is a breakdown of bone which, in times past, has required a surgical procedure. Even so, cures were rare. If, in such a condition, the use of a drug will obviate the necessity for surgery, we must give credit to the drug for that accomplishment and for effecting a cure.

Furthermore, if the drug will permit a more limited type of surgery, as for example in many

Table VI
SHOWING THE RESULTS OF PENICILLIN TREATMENT ACCORDING TO THE PRINCIPAL BACTERIOLOGIC AGENTS ACTIVE IN SURGICAL INFECTIONS

Diagnosis	Total Cases	Results in Percentage					
		Favorable			Unfavorable		
		Excellent	Good	Combined	Questionable	No Effect	Combined
Hemolytic Streptococcus:							
Pure	16	12.5	56.2	68.7	12.5	18.8	31.3
Mixed	85	12.9	49.4	62.3	21.2	16.5	37.7
Coagulase-positive Staphylococcus:							
Pure	47	25.6	61.7	87.3	10.6	2.1	12.7
Mixed	98	10.2	55.2	65.4	23.4	11.2	34.6
Four principal gram-neg. rods:							
Pure	5	0	40.0	40.0	40.0	20.0	60.0
Mixed	95	1.1	49.5	50.6	25.2	24.2	49.4
<i>Cl. welchii</i> :							
Pure	1	0	100.0	100.0	0	0	0
Mixed	28	7.1	35.7	42.8	32.2	25.0	57.2

Table VII
GIVING A LIST OF PROBABLE CAUSES OF FAILURE OF THE 131 CASES IN WHICH PENICILLIN HAD NO EFFECT

1. The presence in mixed culture of organisms capable of producing penicillinase	58
Including:	
<i>E. coli</i>	22
<i>Pr. pyocyaneus</i>	18
<i>B. subtilis</i>	18
<i>B. proteus</i>	15
<i>Aerobacter aerogenes</i>	8
<i>Coli intermediates</i>	3
Other gram-negative aerobic rods	5
2. Tuberculosis	6
3. Tetanus	6
4. Penicillin-resistant staphylococcus	5
5. Penicillin-resistant streptococcus	2
6. Synergism (?) of hemolytic streptococcus and staphylococcus	9
7. Patient in extremis on admission	11
8. Too little	9
9. Too late	7
10. Too conservative surgery	9
11. Diabetes and arteriosclerosis	7
12. Metastatic brain abscess, hemiplegia or meningitis	5

cases of extensive ulceration, particularly the gangrenous types of ulceration; or if with the aid of a drug the natural duration of the infection is shortened, we must give some credit to the drug. That is often hard to determine in any given case, but we know in general the length of time certain surgical infections take. For instance, a carbuncle or a boil has its natural course both with and without surgical treatment. That is within the experience of all of us. If with the aid of a drug that time can be shortened, we must give the drug the credit for aiding in the treatment of that surgical infection.

In times past we have not thought it possible to close an abscess after opening it, but if with the aid of a drug, an infection can be excised or drained and then closed (it has been frequently done with osteomyelitis recently), we must give credit to the agent used in conjunction with the surgical procedure.

All of us who saw service in World War I had the experience of late secondary closure when the wound became clean and free from bacteria. With an undercutting of the edges, closure of the wound was possible and often resulted in prompt healing, but that procedure very often failed if hemolytic streptococci were present. Now if with the aid of a drug those secondary closures can be done earlier or with a greater incidence of success, we must give credit to the drug. Now, therefore, we have certain criteria by which we can determine when drugs are effective in surgical conditions.

There are definite limitations to the use of sulfonamides. There are the bacteriologic limitations, the lack of sensitivity of many organisms, the time limitation when a breakdown of tissue has taken place preventing the contact of the medication with the organisms, the limitation of the impenetrability of thrombosed blood vessels, and particularly the limitations of the so-called inhibitors. We know that broken-down tissue, exudate, pus, and so on, interfere with the local action of the sulfonamides, and probably constituted the chief factors during the war that prevented their favorable action in many cases.

THEN there is the limitation of toxicity, not only general toxicity, but the individual idiosyncrasy that sometimes produces very severe reactions. Last of all, there is the limitation of drug fastness when the organisms become resistant to the drug.

Penicillin, on the other hand, does not have many of these limitations. It is not only bacteriostatic, as the sulfonamides are, but it is actually bactericidal. It is not inhibited by broken-down tissue. It has a wider antibacterial range and is particularly active against the staphylococci. It has the same limitation of time, so that if treatment is delayed it is less effective. The chief inhibitors of the action of penicillin are the organisms which produce penicillinase. These organisms, chiefly of the gram-negative, aerobic rod groups, such as *B. coli*, *proteus*, *pyocyaneus*, and so on, completely

inactivate penicillin in many cases. I believe that the limitation of penicillin in war wounds was largely due to these associated organisms which are almost always present in such cases. That is particularly true in gas gangrene, in which there is almost invariably a mixture of organisms.

TO SUM up, I want to emphasize these things: These drugs are not panaceas. They have their limitations. There are definite indications for their use which should be recognized by all of us. It is absolutely essential at the present stage of our knowledge to learn as much as we can about the bacteriology of any given infection. If we haven't the facilities for determining the causative organism, we are greatly handicapped and our patients may suffer from delay in the proper treatment. Let me plead with you again to know the bacteriology before the treatment of any surgical infection and apply the agent or agents best suited to control the activity of every organism present.

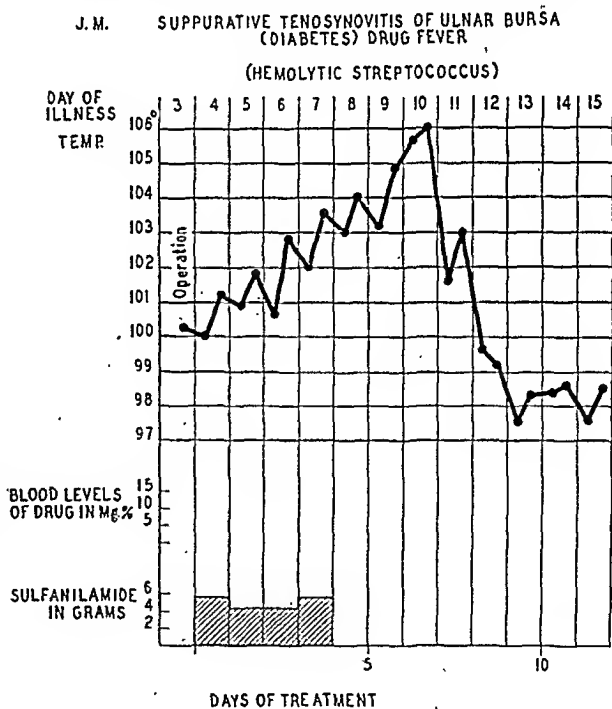
I think it has been demonstrated beyond the shadow of a doubt that the sulfonamides have taken care of the great problem of hemolytic streptococcal infections. Furthermore, we can be pretty sure that penicillin has come in and taken care, to a large extent, of the staphylococcal infections. But there are still infections, particularly with mixed organisms, that are before us as problems to be solved. The antibiotic field has just opened up and we should pursue it with avidity, particularly to find agents which will inhibit organisms not controlled at present by the agents we already have.

Streptomycin is meeting certain types of infection, such as urinary tract infections, but its failure in a great many mixed infections is only too evident. Its great weakness seems to be the development of fastness by organisms which are not completely destroyed. The new antibiotic, bacitracin, with which we are now working, may be able to fill in some of the gaps left by the other antibiotics.

Some temperature curves illustrate more

graphically than in any other way the results of treatment.

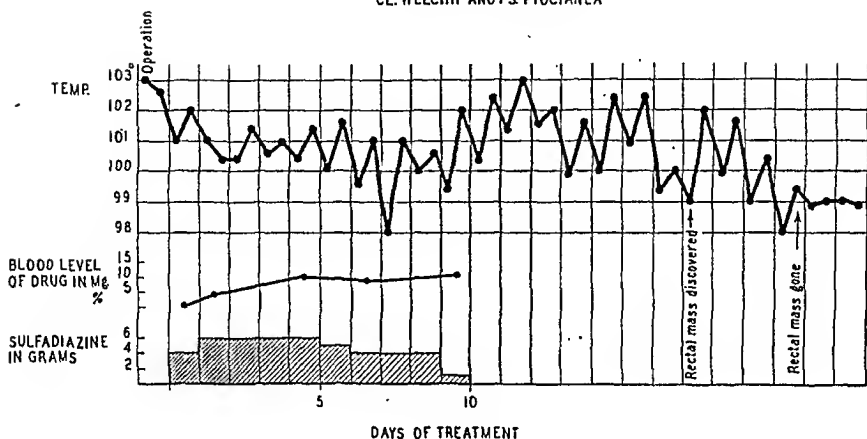
J. M. was a case of a tenosynovitis in the hand of a plumber who had the misfortune to puncture the distal margin of his ulnar bursa with a piece of wire. Infection was very rapid. It spread up through the ulnar bursa. We started treatment with sulfanilamide, but the progress of the infection caused us to proceed with the operation. We opened the ulnar bursa, and then continued with sulfanilamide. The local process rapidly subsided, more rapidly than it would have done without the aid of drug. However, his temperature continued to mount, and it was evident with the subsidence of the local process that he was developing drug fever. The drug was stopped, but still his temperature mounted. He had to be put into an oxygen tent to control his temperature and his restlessness. Then



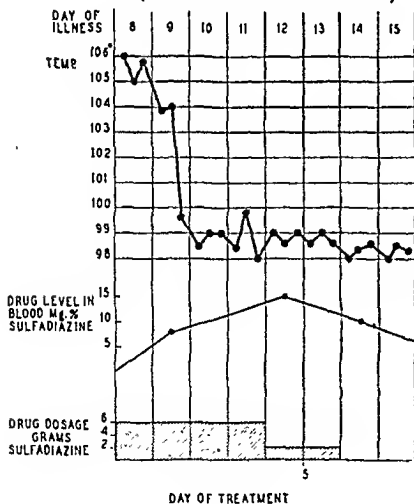
his temperature came down and he made a rapid recovery. Here I think unquestionably the drug aided the surgical procedure in the cure of this man's hand and gave him a perfect result.

Note that this was a hemolytic streptococcus infection.

J. S. ACUTE APPENDICITIS WITH ACUTE DIFFUSE PERITONITIS
(*E. COLI*, NON HEMOLYTIC *STREPTOCOCCUS*,)
CL. WELCHII AND *PS. PYOCYANEA*



M. R. SEPTIC ENDOMETRITIS
(HEMOLYTIC *STREPTOCOCCUS SEPTICEMIA*)

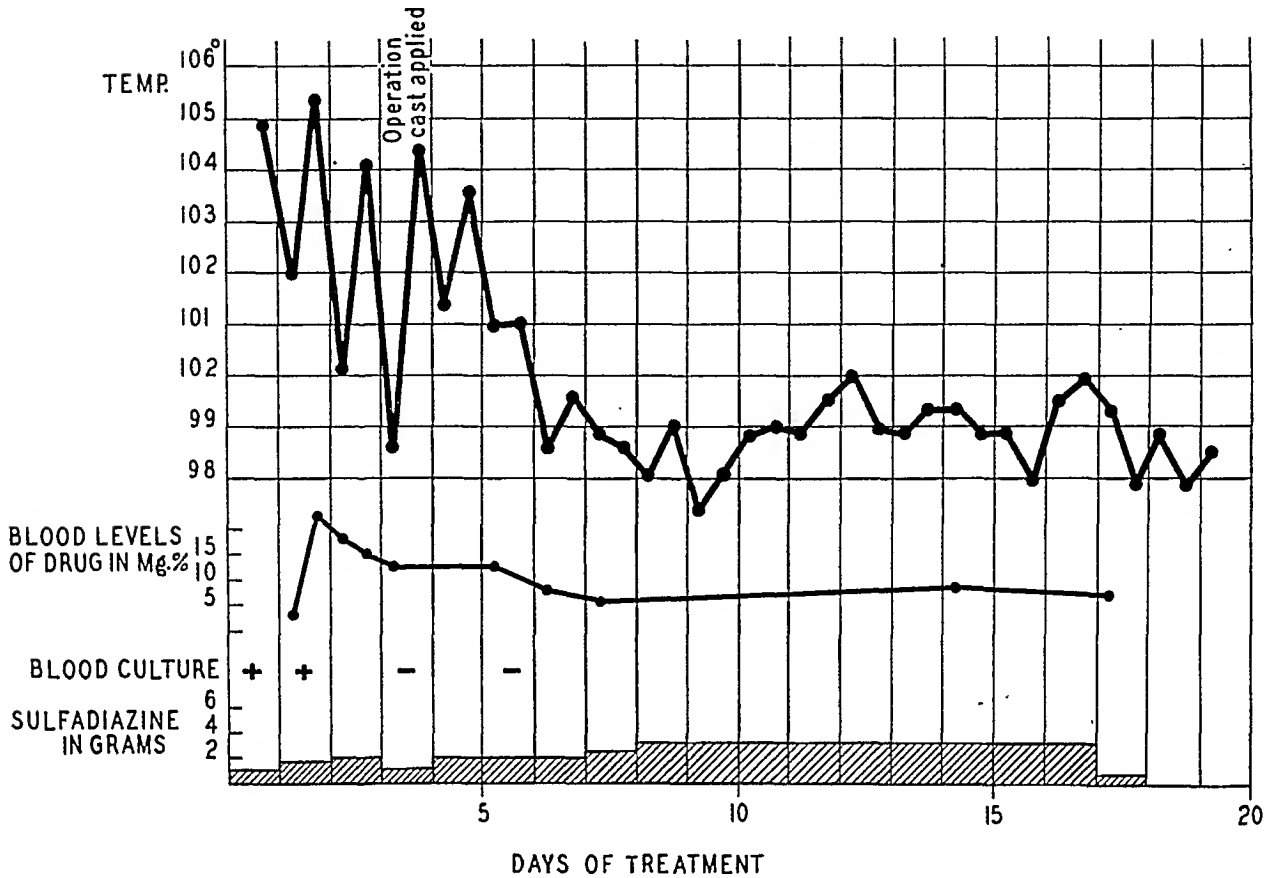


J. S. was a case of appendicitis where drug was given, with a fall in temperature but a secondary rise which we thought was drug fever. We stopped the drug and the temperature came down, then a rectal mass was felt. Without giving more drug that rectal mass disappeared. We had a resolution of a pelvic abscess without the use of drug, and we cannot be sure in this case whether or not the drug was effective in the early stages of the disease.

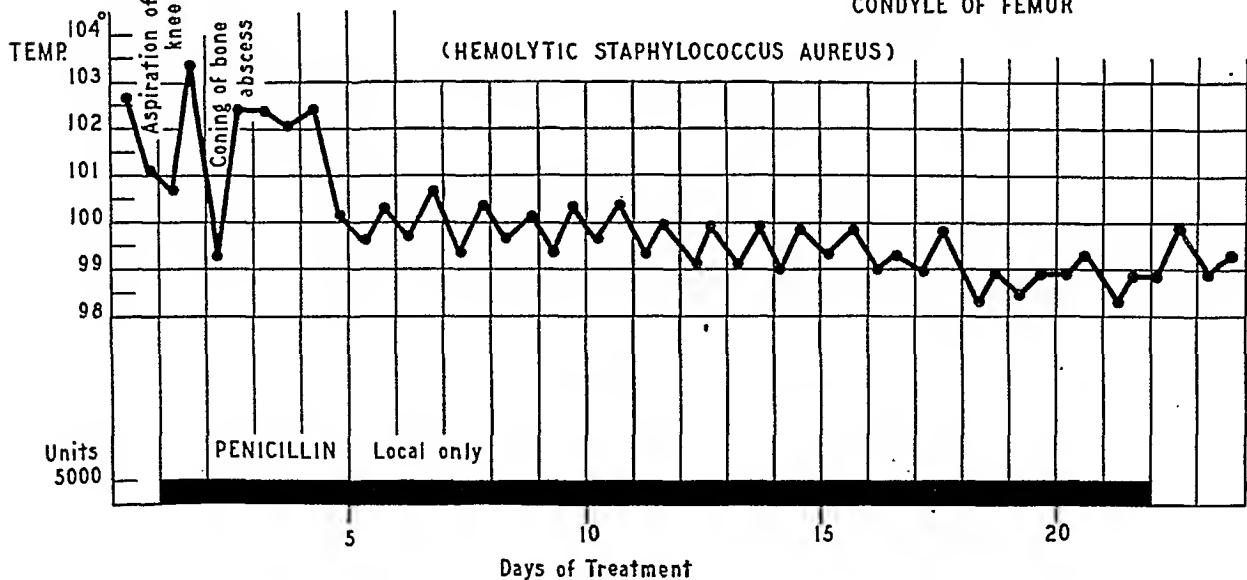
M. R. was a hemolytic streptococcus septic endometritis and it can be seen from the curve that there was a very rapid response to the drug. Again let me emphasize that this was a hemolytic streptococcus infection.

C. V. was osteomyelitis in a child due to a hemolytic streptococcus, with rapid resolution. In this case it was not certain whether the radius or ulna was involved. The radius was operated upon. No pus was found. Later roentgenograms showed that it was the ulna that was involved. In this case the operation was of no benefit, but there was a complete resolution and a regeneration of the bone without the aid of further surgery. A hemolytic

C.V. ACUTE HEMATOGENOUS OSTEOMYELITIS OF THE ULNA WITH SEPTICEMIA
(HEMOLYTIC STREPTOCOCCUS)

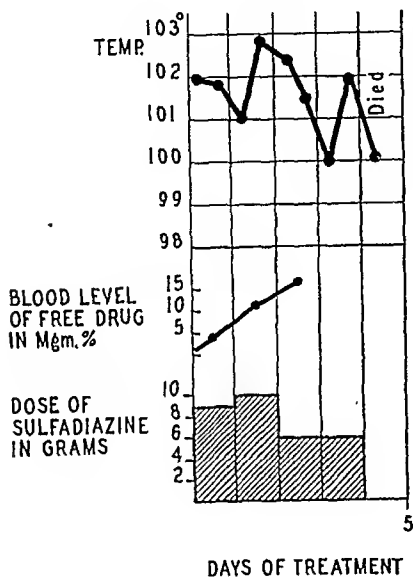


W.D. ACUTE SUPPURATIVE ARTHRITIS OF KNEE - ABSCESS EXTERNAL CONDYLE OF FEMUR
(HEMOLYTIC STAPHYLOCOCCUS AUREUS)



P. W. CELLULITIS OF THE FACE, SEPTICEMIA, ENDOCARDITIS AND MULTIPLE METASTATIC ABSCESSSES

(HEMOLYTIC STAPHYLOCOCCUS AUREUS)



streptococcus osteomyelitis, common in children, is rare in adults.

P. W. was a staphylococcus infection with septicemia in which sulfadiazine, in spite of a rising blood level, had no effect. At the autopsy an endocarditis was found, with multiple abscesses throughout the body. In this case the drug did not change the course of the disease, a staphylococcus infection. As a matter of fact, cures of staphylococcal infections with the sulfonamides were few and far between.

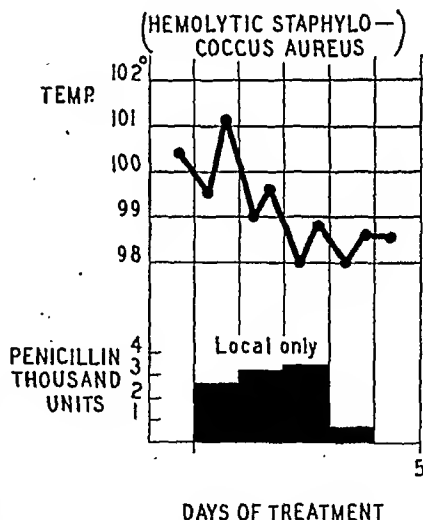
With respect to penicillin, I want particularly to point out that in surgical infections an opportunity is given for local treatment. In case J. O. an abscess of the face responded very promptly to local treatment, and surgery was obviated.

E. S. was a huge abscess of the axilla which responded to limited surgery and the local use of penicillin.

W. D. was a suppurative arthritis of the knee which responded after a single injection of 5000 units of penicillin. There was also a focus in the bone, which was later excised and treated only locally with penicillin. The cavity rapidly filled in with granulation tissue, permitting an early skin graft, and complete healing within 26 days.

I want to say just a word about our new antibiotic, bacitracin. In our study of contaminated civilian wounds we included soft part wounds,

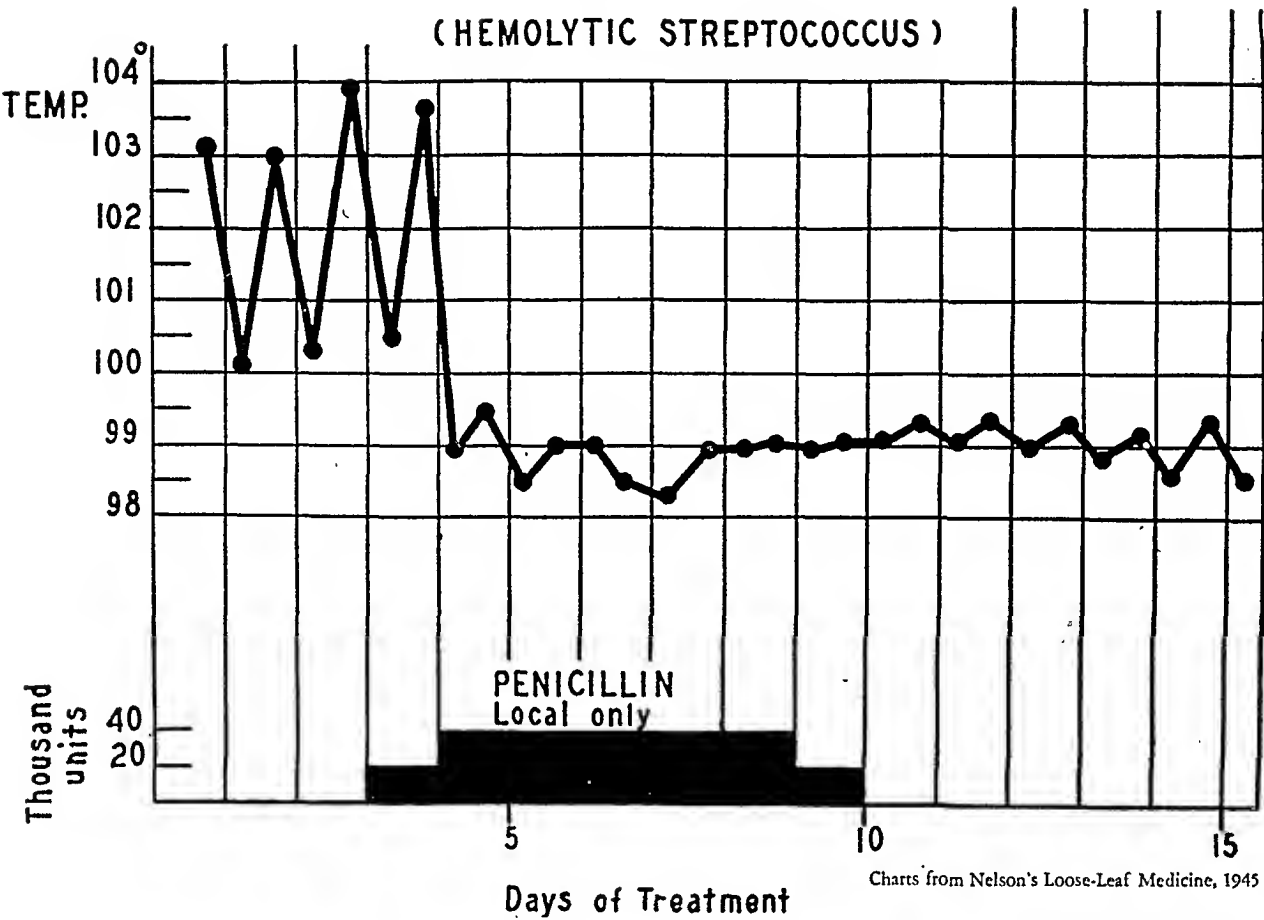
J. O. ABSCESS OF CHEEK AND NECK



burns, and compound fractures. Most of these were badly contaminated with organisms. We were hunting for evidences of antagonistic action in these bacterial mixtures. In one of the compound fractures we found a bacillus of the subtilis group which produces in the culture medium an antibiotic which is relatively non-toxic, and very active, with a wide antibacterial

E.S. ABCESS OF AXILLA

(HEMOLYTIC STREPTOCOCCUS)



range. For the last two years we have been using it locally in the treatment of surgical infections and we are now ready to consider systemic administration.

The table shows 65 cases which have been treated locally with this agent either in solution or in ointment form. We have divided the results as we have with a penicillin study into "excellent," "good," "questionable," and "no effect." The favorable response has been 84.3 per cent, the unfavorable 15.8, in a fairly wide range of localized surgical infections.

I feel the new field of antibiotic therapy has just opened up and will have a very important development in the next five or ten years, when search will be made for agents which will have specific action for the diseases not controlled by the agents now in our possession.

RESULTS IN 65 SURGICAL INFECTIONS TREATED LOCALLY WITH BACITRACIN

Diagnosis	Totals	Results			
		Excel- lent	Good	Question- able	No Effect
Deep abscesses	10	4	6	0	0
Superficial abscesses	7	2	5	0	0
Multiple abscesses of axilla.	1	0	0	1	0
Furuncles	10	5	5	0	0
Multiple furuncles of face..	2	0	0	2	0
Carbuncles	2	0	2	0	0
Infected sebaceous cysts....	7	0	6	1	0
Infected operative wounds..	4	0	4	0	0
Infected burns	1	0	1	0	0
Infected accidental wounds.	1	1	0	0	0
Abscesses of chest wall.....	2	1	1	0	0
Ulcers in old scars.....	3	0	2	1	0
Impetigo	2	2	0	0	0
Stves	2	2	0	0	0
Synergistic gangrene	1	1	0	0	0
Miscellaneous	10	4	4	0	2
TOTALS	65	22	36	5	2
	%	33.9	55.4	7.7	3.1

Serology and Obstetrics

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OBSTETRICAL progress has become increasingly associated with serologic advance. This association began because of interest in blood transfusion, early envisaged as one of the most important obstetrical life-saving aids, continued in the quest of the causes of pregnancy toxemia, and culminated with the discovery of the Rh factor or substance and the relationship of maternal antitoxic substances to fetal injury and death. It now seems quite evident that blood incompatibility, certain pregnancy toxemias, and erythroblastosis fetalis and allied fetal cell injuries all stem from a toxin antitoxin mechanism.

This paper will confine itself to the cell substances, A, B, and Rh, which, among cell substances yet known, seem to be the most important in the causation of the above phenomena.

The argument maintains that the iso-agglutinins, demonstrable in human blood, represent, as in bacteriology, one of the functional arms of specific antitoxic substances, inherited or acquired: the other arms being the lytic and opsonic arms, again as in bacteriology.^{2, 3, 10, 23}

When you mix incompatible bloods, the red cells of the blood containing the agglutino-gen or agglutinogens are agglutinated by the spe-

cific agglutinin or agglutinins in the other blood, but the basic reason for the presence of the agglutinin or agglutinins lies in the fact that this blood comes from an individual whose cells are susceptible to the toxic action of the blood substances represented by the agglutinogens—the agglutinogens being but structural parts of these substances. The blood of a donor is incompatible with the blood of a recipient if it contains cell substances strongly toxic to the cells of the recipient and the blood of the recipient contains specific antitoxic substances, inherited or acquired.

The nearest approach to blood transfusion in nature may occur, at times and in infinitesimal quantities, between the fetus and its mother. If this occurs, and the fetal blood, due to the bisexual mechanics of human reproduction, and under the laws of heredity, contains one or more of the cell substances, A, B, or Rh, not possessed by that mother, and they can gain access to her cells, a toxin antitoxin battle ensues. If the mother is not adequately protected by a hereditary complement of specific antitoxic substances, or her cells are not vigorous enough to manufacture antitoxic substance actively, her organism may show characteristic signs and lesions grouped under the obstetrical caption of preeclamptic toxemia. If her antitoxic substances become too strong, they may in turn injure or destroy the fetal cells containing the toxic cell substances against which the antitoxin is specific, and thus injure or kill

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the fetus. The following of iso-agglutinin titers, both before and after delivery, in preeclamptic toxemia and in cases involving the erythroblastosis problem, has strongly supported this hypothesis.¹³

This obstetrical view permits a reasonable assumption in explanation of why, under the mechanism of heredity, and in our infinitesimal segment of time in human evolution, the group O mother inherits the anti-A and the anti-B agglutinins; the group A mother, the anti-B agglutinin; and the group B mother, the anti-A agglutinin. They contribute to her safety in the event that she bears a child whose cell substances are toxic to her cells, and these toxic cells and their circulating antigens can gain access to her blood. These agglutinins, arms of specific antitoxins, militate against her only in the event of gross transfusion of toxic blood. Gross transfusion of blood between individuals was not envisaged by nature.

In gross transfusion, and even in the intramuscular injection of blood, we should think in terms of toxic and nontoxic blood, as well as in terms of incompatible and compatible blood.^{6, 20} Reactions to some intramuscular injections, and pathology found in some cases of delayed transfusion deaths, give glimpses of true toxic action. It is pathology similar in kind to preeclamptic pathology. In rapid transfusion deaths the effects of the toxin have not had time to manifest themselves, or they are entirely obscured by red-cell agglutination and red-cell detritus.

The following question immediately suggests itself: If this suggestion concerning the agglutininogen and agglutinin setups of the blood groups is correct, why is it that the Rh antitoxin is not inherited by the Rh-negative individual? The most logical answer, to date, would seem to be that the Rh substance has entered the species at a date too recent in evolutionary time to allow of its antitoxin becoming yet inheritable. If one will analyze the blood group setups from an ontogenic viewpoint, one will see that although the A and B substances, as shown by Kemp,⁷ can be demonstrated in the fetus as early as the thirty-seventh day of gestation, the fetus' true complement of agglutinins

or antitoxic substances does not appear until well after the two hundred and eightieth day.^{22, 23} From this fact it would thus seem logical to argue that it takes in the neighborhood of eight times longer for an intraspecies specific antitoxic substance to become inheritable than it does for a cell substance to become inheritable.

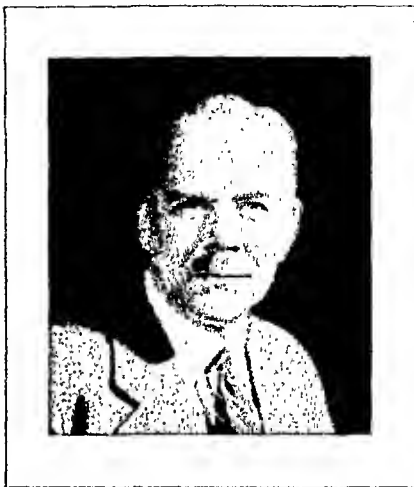
IT HAS long been sensed by obstetricians that if toxemia of pregnancy is ever due to a fetal toxin—and clinical and pathologic data have increasingly pointed to this likelihood—the final proof would have to lie in the field of serology. For this reason every serologic lead has been followed attentively. In 1905, Dienst, due to similarities between pregnancy toxemia pathology and transfusion pathology, suggested that toxemia was caused by incompatible fetal blood gaining access to the mother. It can be seen in retrospect that this hypothesis failed of proof and was discredited because evidence was not then available that would allow the concept of the toxicity of the cell substances represented by the agglutinogens. The hypothesis was based on the concept of a static agglutinin, a mere hereditary characteristic, and was founded on the effect of agglutination of fetal blood upon the maternal organism.

It can be seen that in later serologic investigations of pregnancy toxemia, the therapeutic importance of gross blood transfusion has been so great, and the original definitions of the factors governing its safety or danger have been so adequate in this particular field, that our minds have been polarized, so to speak, and have been particularly obtuse in sensing the real nature of the factors involved. And again, even to this day, unless the mind is gradually accustomed to the light of new knowledge, the first reaction is to close the mind and oppose any change of viewpoint that would affect the original concept of the blood groups and their relationship to blood transfusion.

The idea of Dienst was resurrected in 1919, and pursued for many years, with the result that there was no generally accepted change in the previous conclusion that the theory of

fetal blood incompatibility as a cause of pregnancy toxemia was untenable. McQuarrie,¹⁸ in 1923, reported that he found pregnancy toxemia sixteen and one-half times more frequent, where fetal blood was incompatible with that of the mother, than where it was not. It was felt, however, that these findings suffered from the error inherent in chance sampling, due to the unavailability of a large number of cases, because, under similar conditions, both before and after this publication, other investigators could find no significant difference between the number of group incompatible fetuses associated with the finding of toxemia in the mother, and the number not associated with toxemia. Again they could find no significant difference between the number of toxemias bearing group incompatible children and the number of toxemias in which fetal incompatibility could not be demonstrated. In the light of what was then known, an analysis of these findings could logically result only in a decision against the theory of fetal group incompatibility.

IF ONE reanalyzes the figures in the light of present knowledge, he realizes that, given any number of incompatible fetuses, and viewing the maternal protection that is afforded by fetuses that are not secretors, the protection of the placental barrier, and the protection afforded by a complement of inherited antitoxins, it would seem highly significant that 50 per cent of the mothers bearing these fetuses would develop toxemia. Furthermore it becomes significant that when only the A and B toxins are involved, they account for one half of the toxemias. If the Rh substance is added, the number of toxemias not demonstrably associated with a fetal toxin becomes smaller. As it has taken forty years to demonstrate an additional substance as important as the Rh substance, it is likely that other cell substances, important in disease, are still unknown. This assumption is rendered more likely by irregular crossmatching reactions not at present explainable. Today, it would seem that we are faced with the problem of how sure we can be that a toxemia, not showing a demonstrable fetal



Underwood & Underwood, Washington, D. C.
Rae T. LaVake

toxin origin, can be placed in the category of a toxemia due solely to cardio-vascular-renal inadequacy, either from heredity or disease. And, among the possible diseases, a previous toxemia must be included, and possibly antitoxin injury in fetal life.

The first data that led to a suspicion of the true character of the agglutinogens and agglutinins, and the substances they represented in blood were found in an article of Jonsson in 1936.⁵ The data showed that if postpartum agglutinin titers were made on group O women, the anti-A agglutinin titers of women bearing group A children averaged higher than their anti-B agglutinin titers; and the anti-B agglutinin titers of women bearing group B children averaged higher than their anti-A agglutinin titers.

It seemed that these data might reasonably be interpreted as pointing to a functional reaction of an antitoxin in the mother to a toxin in the fetus. However, this interpretation was cast aside because it was not deemed to be within the canons of serology to associate a blood

group agglutinin with a toxin or an inherited blood group agglutinin with an antitoxin. And besides, the fact that there was no significant increase in the number of toxemics showing an associated incompatibility with the fetus over the number showing no incompatibility, seemed to count out any involvement of elements associated with incompatibility.

As it still appeared increasingly evident from clinical observations that, in pregnancy toxemia, we were dealing with a fetal toxin, it was determined to approach the matter from a different serologic angle. To this end, a maternal intradermal skin test was devised, designed to show, in ways suggested by the Mantoux test, that whenever positive, it could be reasoned that a toxin was coming from the fetus and that the mother was immunized to this toxin.¹² The positive results of this test in toxemics seemed to raise the fetal toxin hypothesis to a high degree of probability, especially because they constituted forms of proof by prediction, a very strong form in the proof of a hypothesis. However, the work was soon given up because, even when positive, it failed to suggest the identity and nature of the toxin, and it could be taken only after the birth of the child. It was felt, however, that when negative, the test might be of diagnostic and prognostic value in placing the toxemia in the category of a toxemia arising wholly from a cardio-vascular-renal inadequacy, either due to heredity or disease.

THEN came the real illumination. It began with a report by Levine and Stetson in 1939,¹⁵ of the iso-immunization of a mother by the fetus; continued with the discovery of the Rh factor by Landsteiner and Wiener,⁸ and the demonstration, by Wiener and Peters,²⁴ of the danger of iso-immunization with the Rh factor in transfusion; and culminated in the work of Levine, Katzin, and Burnham,¹⁶ Javert,⁴ and others, showing the relationship of the Rh factor or substance to erythroblastosis fetalis and allied fetal injury. It was found, as experience increased, that the A and B substances could bring about a similar train of phenomena when the blood of the mother and fetus were similar

from the Rh standpoint, thus showing that these substances could act similarly as toxins. It was found that, in about 30 per cent of the cases showing erythroblastotic phenomena, pregnancy toxemia was manifest.

Now when the light of this work was thrown upon toxemia, it was found that by titrating maternal agglutinins both before and after delivery, one could predict, before delivery, the blood substances implicated if they were the A, B, or Rh substances, by the functional changes in the respective maternal agglutinins; one could recognize a functional relationship between the severity of the manifestations of toxemia and the titer of the agglutinin (ante-partum, the lower the titer the more severe the manifestations tended to be; and, postpartum, the higher the rise of the titer, the more quickly the manifestations of toxemia tended to resolve).¹³ In other words, we were witnessing a mechanism and train of phenomena paralleling those operating in snake venom poisoning or bacterial toxemia. It became apparent that the concept of the blood groups and blood group incompatibility had been dependent upon inherited antitoxic substances; the agglutinogens and so-called natural iso-agglutinin of the group being merely functional parts of a larger potential functional mechanism—a toxin antitoxin mechanism.

It would seem that the findings of Levine, Katzin, and Burnham can be interpreted only as an example of the quite generally accepted toxin antitoxin mechanism enunciated by Ehrlich. We are dealing with a functional toxin antitoxin mechanism and not with mere static blood characteristics that make it possible to differentiate types of individuals.

Assuming this to be a correct interpretation, it was predicted from analogy that one should be able to injure and kill a rattlesnake by the injection of rattlesnake antivenom. With the aid of Dr. W. J. Breckenridge, Director of the Museum of Natural History, of the University of Minnesota, this experiment was performed. Snakes of two sizes were killed, and slides of their normal vital organs prepared and read by Dr. W. R. Koucky, pathologist, Minneapolis.

Two snakes of corresponding age and size were then injected, each with 15 cc. of rattlesnake antivenom. In both snakes, within fifteen minutes, every muscle became clonically convulsed. The smaller snake, as would be expected, appeared to be the more seriously affected. In addition to the clonic contractions of its individual muscles, it assumed a perfect circular attitude, snapping convulsively at its vibrating rattles. It showed periods of apparent normality but died in eighteen hours. The cells of its vital organs showed suggestive signs of injury. The larger snake after several hours seemed to recover entirely, but it was killed in five days and the cells of its vital organs also showed suggestive signs of injury.

A snake, similar in size to the larger snake in the previous experiment, was given 15 cc. in divided doses of 1 cc. each every other day for a month. This snake showed no visible reaction, but the cells of its vital organs showed suggestive signs of injury. The term suggestive must be used pending thorough corroboration of abnormality and cause.

This work is being pursued to determine whether, after a long subjection to fractional dosage, a snake will eventually die, as is the case with the erythroblastotic infant, and show characteristic pathology. It is also hoped that it will throw some light on what is now suspected, namely, that though we may ostensibly clear up manifest pathology and save the lives of some erythroblastotic infants by blood transfusion, they may be handicapped by basic lesions of vital organs, basic lesions that cannot be cured. This basic injury may account for many abnormal conditions of each and every vital organ, conditions that we have previously attributed to hereditary causes.

It would seem that a host's immunization to snake venom differs from a mother's isoimmunization to a toxic fetus only in phylogeny. Both poisons come from cell substances. Lehrs and Putkonen, in 1930,¹⁴ discovered that some humans secrete their A and B cell substances in their saliva, where it is found in higher concentration than obtains in the red blood cells. Some individuals do not secrete their cell

substances. The former were called secretors by Schiff and Sasaki in 1932,²¹ and it was found that 80 per cent of humans were secretors and 20 per cent were nonsecretors. The basis of this difference lies in the fact that in secretors the cell substances are in aqueous solution, whereas in nonsecretors the cell substances are in lipid solution and can be extracted only with fat solvents. The hereditary character of these systems was established by Schiff and Sasaki. One may look upon it as a phylogenetic hangover. Thus, to a degree, secretors may be technically poisonous to certain other individuals. The peculiar appearance of some human bites corroborates the likelihood of this toxin antitoxin setup.

SNAKE VENOM is merely the concentrated saliva of the snake. That it comes from cell substances present in most, if not all, of the cells of the snake seems to be predictable from the action of each individual muscle cell of the snake when attacked by antitoxin. As one looks along the snake, reacting to antitoxin, the disorderly individual contractions of the muscle cells give the appearance of the surface of a lake ruffled by a slight breeze. At the same time the cells of the vital organs are injured. Thus the analogy between a toxic fetus and its mother and a poisonous snake and its host and the analogy between the reactions of the fetus and snake to antitoxin attack is not merely fantastic, but founded upon basic similarities that are more important than their dissimilarities, which, in logic, establishes the strength of an analogy.

Unless one distinctly visualizes the protective variants operating in behalf of the mother and in behalf of the child in the toxin antitoxin battle, one's average of perplexity over the correct interpretation of the absence or presence of disease manifestations, and over the actions of the agglutinin titers, will be increased.

The mother is protected by the relative larger bulk of her cells. This bulk operates to fractionate the dose of toxin to each cell. Again, no matter what the antitoxin generating power of each cell, the total amount of antitoxin developed is directly proportional to her bulk.

Upon the latter fact is based the estimation of the proper dosage of antivenom in snake poisoning. The dose has to be larger in children than in adults, not only because of the larger fractional dose of the toxin to each cell, but because the smaller bulk of cells of the child cannot afford sufficient additional aid by actively secreting antitoxin.

The mother receives the protection afforded by a normal placenta. And she is protected by inherited and acquired antitoxins. It is likely that she is protected to a certain extent if her fetus is a nonsecretor. But whatever the interactive protective or deleterious relationship between the secretor or nonsecretor properties of mother and fetus may be, can as yet only be conjectured. She seems free from any danger of antitoxin damage, because, as far as is known, whatever agglutinins are found in the fetus at birth come from the mother by filtration or some such method.^{22, 23}

The fetus, it would seem, is relatively protected from maternal antitoxins by the fact, established by Kemp,⁷ that fetal red blood cells are five times more resistant to agglutination than are adult cells. The same ratio may apply to the resistance of fetal red cells and fixed cells to the lytic or deleterious action of maternal toxins.

AN IMPORTANT problem, which we know little about at present, is whether maternal toxic blood substances can reach the fetus and damage the fetal cells as fetal toxic blood substances tend to damage the maternal cells. This may account for many variations of fetal pathology. Clinical observations support this likelihood. To speak in traditional hematologic parlance, if maternal agglutinins can reach the fetus, and fetal agglutinogens can reach the mother, maternal agglutinogens should be able to reach the fetus. If so, it would seem that the fetal cells, unless especially resistant, as they are known to be to agglutination, should be easy prey. That they are likely to be especially resistant is evidenced by the number of apparently normal group O fetuses that are born to group A and group B mothers.

That the placenta acts to a certain extent as a barrier to maternal antitoxins is evidenced by the fact that though maternal agglutinins may be found in the fetus at birth, their titer is always lower than that found in the mother.²⁵

In following antitoxin titers it is often baffling to have an agglutinin suddenly decrease in titer or even disappear. This phenomenon introduces another problematical variant, namely, the antibody absorptive power of the fetus. If the fetus be a secretor, all the fetal blood substances combined, in fixed cells, blood and all secretions and excretions, amniotic fluid included, may technically absorb huge amounts of antibody.

In regard to the toxemia problem and the toxin antitoxin setup, several observational sidelights are interesting. Theoretically the placenta is the front line of the toxin antitoxin battle. When one examines a placenta he is viewing the immediate remains of a possible toxin antitoxin battleground. It seems likely that many of the so-called infarcts mark leaks in the placenta that are filled with dead agglutinated attackers, the differences in coloration marking the progress of subsequent hemolysis. The gross and microscopic manifestations of placental aging and pathology have been comprehensively presented by Bartholomew and Kracke.¹ It would seem that the cause of some of these findings can best be explained from a toxin antitoxin viewpoint.

This process can be logically assumed to operate both for the weal and woe of mother and fetus. For the mother, it first tends to shut off toxic attack, but later under lysis results in the increase of liberated toxin. For the fetus, it first diminishes antitoxin attack, but tends to separate the fetus from its source of oxygen and sustenance,¹⁰ and impedes its channels of elimination. The result may be premature delivery, before lethal or serious damage has been sustained by mother or child, or death and abortion of the fetus.

Infarcts are present in some degree in practically all placentae. Some of these infarcts may be due to mild toxic substances which are

known to be acted upon at times by agglutinins, inherited or acquired in other bloods, but apparently are little, if at all, implicated in toxemia. However, there has long seemed to be an increasing belief that widespread gross infarction correlates so highly with toxemia that it is likely an element in the cause of toxemia.^{10, 11} If one follows anti-A, B, or Rh titers, he is more likely to come to the conclusion that a toxin antitoxin setup is the basic cause.

Antibody titer findings also seem to corroborate the clinical observation that general infections antedate and often precipitate toxemia by causing placental infarction, which infarction can be predicted and later computed as having occurred during the time of the infection.^{3, 11} Infection as a cause of infarction has been called next to impossible by some, because bacteria and the usual signs of infection are not found around infarcts. Now, if one is following antitoxin titers, if a severe infection occurs, the titer strength of these antitoxins may be seen to rise to many times their previous level, and subside to their preinfection level when the infection resolves. It would seem highly probable, at least theoretically, that this rise of antitoxin strength would make infarction more widespread and conspicuous. If this be true, and the final necrosis of the infarcts increases the toxemia, it would seem justifiable to assume that the elimination of focal infection and the prevention of general infection would be indicated as prophylactic measures against toxemia. By the same token, this jump in antitoxin titer may be an added factor in accounting for the high correlation between infection and the death of the fetus and abortion, both by the direct action of the antitoxin on the cells of the fetus, and by placental infarction.

Since the work of James Young in 1914,¹² there has been a feeling that premature separation of the placenta and pregnancy toxemia have some causal relationship with each other. Attention to the blood toxin antitoxin setup makes it seem highly probable that they both stem from the same toxin antitoxin back-

ground, when they are related at all. One of the interesting features of this work is that you can test out the likelihood of toxin antitoxin background on your outstanding cases of toxemia and premature separation, from the beginning of your practice, if the *dramatis personae* are still available.

If one has made it a point to be present, if possible, whenever the abdomen has been opened, for any reason, in pregnancy toxemia or premature separation, he likely has concluded that the bizarre petechial and ecchymotic findings, unexplainable by anatomic analysis, can be accounted for only on a toxic basis. It is no exaggeration to say that, at times, the only clinical picture comparable to the pelvic findings can be found in the vicinity of snake bites.

It is a belief that the best approach to this whole matter is to insist on knowing the A, B, and Rh status of husband and wife as we insist on knowing the Wassermann status. It can all be accomplished with one drawing of blood and thus does not necessitate any additional inconvenience. It can be done very advantageously at the laboratory of the hospital chosen for confinement. It is inexpensive, and once obtained, need not be repeated in future pregnancies.

FAR from producing unnecessary anxiety, experience proves that it has exactly the opposite effect. Popular articles and uninstructed social discussions have inspired an almost universal dread of the terrible Rh factor. This dread raises its head where you would least expect it. Invariably, both husband and wife express relief that consideration is being given to the blood condition, and they cooperate enthusiastically in having the tests made. No matter what the results of the tests, it gives one an opportunity of allaying inordinate fears and of convincing husband and wife alike of the infrequency of any disaster, because of nature's safeguards.

It gives the physician a feeling of reasoned preparedness. Its usefulness will be found to be infinitely more frequent than the Wassermann

knowledge, which of course is a prerequisite in proper care.

When, from principles of genetics, one can be quite sure that the infant cannot inherit an A, B, or Rh substance known to be potentially toxic to that mother, he can likewise be reasonably sure that he will not encounter pregnancy toxemia, premature separation of the placenta, or erythroblastosis due to a toxin antitoxin background. The likelihood of abortion is diminished, even if an acute infection occurs. Other setups can be marked "Watch" and extra care taken in their supervision.

One of the greatest advantages of this approach is that it permits the building up of sources of Rh-negative blood of every blood group that can be turned to, in case of need.

In an Rh-negative woman with an Rh-positive husband, especially if the slightest sign appears that can be attributed to a beginning toxemia, it is well to test, at regular monthly intervals, beginning at the sixth month, for the presence of an Rh antibody, if only to make preparations for the immediate examination of the infant's blood at birth and to line up appropriate donors if the antibody appears. One is often agreeably surprised to find a normal baby. Such experiences make it evident that, in general, one should not interfere obstetrically until one child has been born severely diseased. If you do, in the long run you will likely lose more normal babies from prematurity than you will save by intervention and immediate treatment, if this is found to be necessary. It is quite different after a history of one serious injury or disaster. Then, if in the next pregnancy the Rh antibody appears and rises, or the A or B antibodies are at fault and rise, one can be quite sure that he is dealing with another fetus of like toxic status, and, after one can be reasonably sure that the fetus has reached the age of viability, it would better be separated from the mother by Caesarean, or rupture of the membranes according to the presentation, position, station of head in the pelvis, and the condition of the cervix. The chance of success is much reduced below the normal low average of success,

if what is known as a blocked antibody obtains. Where the latter obtains, most of these fetuses succumb before they reach the age of viability.

IF, FOR any reason, one does not like the all-out approach, above mentioned, an excellent and simple approach is to examine routinely the blood of newborns. Dr. W. R. Koucky, pathologist, has been doing this for five years at Abbott Hospital, Minneapolis. Any child with ten or more erythroblasts, to 100 leukocytes counted, and with a hemoglobin approaching 100, or below 100, is considered suspicious. The aim of this is not only to direct treatment, if necessary, but to call attention to the advisability of examining the blood status of husband and wife as a basis for future decisions. As erythroblastotic disaster very seldom appears in early pregnancies, and sometimes not even after iso-immunity has been demonstrated previously, this approach is excellent.

Some contend that there is no evidence that toxemia is caused by the Rh substance. A 30 per cent correlation would not seem to bear out this opinion. Furthermore, it is a belief, founded on clinical observation and titer studies, that many slight signs of toxemia are overlooked or not recorded, and that absence in 70 per cent of cases is due to a combination of overlooking slight signs and to the likelihood that the women in these instances are completely protected by the height of the antitoxin strength.

From the toxemia standpoint, the main importance of this whole argument is the direction that the findings give to the development of specific antitoxins to be used, in behalf of the mother, either after the intrapartum death of the child, or after the delivery of a live child, especially in antepartum and postpartum eclampsia. This direction is being followed.

In 1926, McMahon¹⁷ published a preliminary report of the treatment of ten cases of pre-eclamptic toxemia, with astonishingly and conspicuously good results, by the administration of serum taken from a woman who was just recovering from a toxemia. His comments were, "We are unable to offer any satisfactory ex-

planation explaining these results, etc." He was not alone in not being able to prove the mechanism. But it did seem that if the results had any basis of cause and effect, it must be a toxin antitoxin basis. But what was the antitoxin and to what substance was it antitoxic? It was not suspected that the results had anything to do with the agglutinogens or the agglutinins, because by the canons, they were merely inherited properties or characteristics that permitted the division of humans into four groups, and had to do mostly with incompatibility and blood transfusion.

Well, McMahon's observations went by the boards just as had Dienst's theory of incompatibility, because with knowledge then at hand, the mechanism was not amenable to proof, and besides, it just did not always work. Present knowledge suggests that one could as reasonably, with any hope of success, give a woman suffering from an A substance toxemia, a B antitoxin; or a B and A antitoxin; or an Rh and A or B antitoxin, as he could give a person bitten by a snake whose venom is of the neurotoxic variety an antivenom operating against the hemotoxic variety.

Now, in closing, let us look at the obstetrical problems presented by transfusion.

It is true that by careful crossmatching, aided by Levine's incubational method and checked by serum suspension of red cells, transfusion

can be made quite safe, even if the woman had been iso-immunized by a pregnancy or a transfusion by any known or unknown substance. However, what is considered of great importance by obstetricians, who have had any experience with erythroblastosis, is the danger of the future unnecessary increase of this disease if the Rh status of women is not considered before transfusion. It has been estimated that a transfusion is ten times more likely to iso-immunize a woman than is a pregnancy.

In the past few years, the frequency of transfusion in the proper interests of therapeutics, has increased tremendously. As yet, the indications for the proper use of transfusion in obstetrics have not reached the saturation point. But this very increase raises the apprehension that, unless more care is taken in giving only Rh-negative blood to Rh-negative women, except in extreme emergency, we are surely going to see a marked increase in erythroblastosis and allied fetal injury. Much of the obstetrical increase in transfusion is accounted for by the demands for transfusion in inevitable abortion in young women. There is no intent of exaggerating the danger that these young women may be iso-immunized with dire consequences to their future ability to bear healthy or viable children, but it does seem that this possibility should be continuously emphasized.

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The Treatment of Diabetic Acidosis and Diabetic Coma

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THERE is no one accepted technique for the treatment of diabetic acidosis and coma at present. Therefore, I can only discuss the method which I have used and with which I have had the greatest experience. It is not presented as the most perfect plan of treatment, but as a plan which has given satisfactory results.

DEFINITION

Diabetic acidosis—This is a clinical picture in which a patient with diabetes develops increased thirst, frequency, weakness, acetone breath, nausea, vomiting, abdominal and chest pains, soft eyeballs, and other evidences of dehydration; and air hunger (Kussmaul breathing). The laboratory studies will reveal a glycosuria, ketonuria, hyperglycemia, leukocytosis, and a low carbon dioxide combining power. *However, the patient is conscious.*

Diabetic coma—When a patient with diabetic acidosis loses consciousness, *then, and only then*, is the diagnosis of diabetic coma made. Such a patient may be semiconscious—that is, he will respond to stimuli, but may be unable to take fluids or answer questions—or he may be unconscious so that he does not even re-

spond to stimuli. I agree with Owens¹ that the term “diabetic coma” should be used only with those patients in ketosis, whose mental state has become one of unconsciousness. It is wholly a *clinical* diagnosis. True, the carbon dioxide combining power is usually low. This indicates only the degree of the acidosis, *not* the mental status of the patient.

DEVELOPMENT OF THE CLINICAL PICTURES AND THEIR MANAGEMENT

The mild case—Often a trained diabetic patient under observation will carry on, feel well, hold his weight, and be free from symptoms; though he has glycosuria, he will not show acetone in the urine. At times, during a slight upper respiratory infection, a gastro-intestinal upset, or an extreme sunburn, or even without apparent cause, the patient's thirst will increase, his urinary output will rise, and acetone will be found in the urine. The qualitative reading of the reaction may be 1 to 4 plus. Such a patient is not hospitalized. He is usually familiar with the tests for acetone and sugar and can follow his treatment at home. He is then told to follow these directions:

1. Test your specimens every time you void, for sugar and acetone.
2. If acetone is present, take regular insulin in amounts depending upon the quantity of sugar

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found in the urine. That is, if the test is yellow, brown, or orange (4 plus) take 25 units; if the test is green with yellow sediment, take 15 units; if the urine is blue or free from sugar, take the juice of an orange.

3. Drink all you can—water, milk, fruit juices, ginger ale.

4. Take salty broths and if they are not available, two salt tablets (1.0 gm.—XV grs.) every two hours.

5. Continue this routine until three consecutive specimens are acetone-free. If acetone persists and you feel nauseous or vomit, come to the hospital at once.

By means of this home treatment the ketosis clears rapidly, and as the underlying cause improves, the patient can resume his former regimen. In cases where the ketosis appears without apparent cause, I have learned that an increase of the daily dose of insulin remedies the situation.

Case 1 refers to a typical clinical picture of acidosis.

CASE 1

From 6:45 P.M. to 11:30 P.M. —25 units of insulin every half hour as specimens contained 4+ sugar and 4+acetone. WBC 25,800. Blood Sugar 425. CO₂—20 on admission. Patient received 1000 cc. 5 per cent glucose in saline at once and 7 doses of 50 cc. each of salty broth about 1 hour apart as well as about 1710 cc. of fruit juices. Water was given ad lib. Discharge Diet, P60 P60 C200.

Time, A. M.	Insulin Units	Sugar	Acetone	Diabetic Acid
12:00	25	4+	2+	0
12:30	25	4+	1+	0
1:00	25	3+	0	0
1:30	10	2+	0	0
2:30	0	1+	0	0
3:00	15	0	0	0
4:00	15	0	0	0
5:00	15	0	0	0
6:00	0	0	0	0
7:00	0	0	0	0
8:00	0	0	0	0

The moderately severe and the severe case—

Before presenting a description of this group I want to state categorically that *every newly diagnosed* diabetic with ketosis, regardless of the severity of the case, should be hospitalized, chiefly because of the patient's lack of training. Because of hospital overcrowding, however, I have treated these cases at home. Here the help of a nurse or a member of the family was urgently needed. I taught them the routine of testing, left definite written instructions, kept in touch by telephone at hourly intervals, and made calls as often as I could. There were no dire consequences.

THE moderately severe case developing keto-acidosis and coma may reveal the following pattern. The patient develops a sore throat or some other infection. His temperature rises, he develops malaise, and he has no desire for food. Since he has decided not to eat, he sees no necessity for taking insulin as he fears a reaction. He may not eat for one or two days or more, subsisting on fruit juices and other fluids and still reasoning that under these circumstances insulin is unnecessary. Soon he observes an increase in thirst and notes frequency. He then develops aching legs, weakness, restlessness, and, perhaps, some somnolence. He carries on. Soon there appear epigastric pain, nausea, and vomiting. His heart beats rapidly, and it becomes difficult for him to breathe. He or some member of the family becomes

alarmed, and either a physician is called or the patient is taken to the hospital. Often no medical aid is sought until the patient is unconscious or has been for many hours. When such a patient is admitted to the hospital, the infection will be treated by any of the modern chemotherapeutic agents. His diabetic acidosis or coma or both will be treated as follows:

1. If the patient is unconscious, insert a catheter into the bladder and clamp it. This will facilitate getting samples of urine for analysis.
2. Give 25 units of regular insulin subcutaneously every half hour until the clinical symptoms of ketosis begin to disappear and the urine becomes acetone-free.
3. If the patient can take and retain fluids, give 2 or 3 glassfuls (200 cc.) of fruit juice every half to one hour. Salty broths and other liquids are given as frequently as the patient desires.
4. If fluids cannot be given by mouth, give 1000 cc. 5 per cent glucose in saline at once, rapidly. The infusion is then continued at a slower rate until the oral route can be used. In any continuous intravenous therapy, great care must be exercised to prevent overloading

the right heart. This hazard is present in the older diabetic with arteriosclerosis and the young cardiac.

5. After the urine has become free from acetone bodies continue giving 25 units of insulin and 2 glasses of orange juice every two hours for 4 or more doses.

Of 100 cases of diabetic acidosis and coma, so treated, there were 7 deaths of which only 2 were due to the acidosis per se, and of these 2, one was highly insulin-resistant.

Case II is that of a patient who had diabetes for 12 years.

KETO-ACIDOSIS DEVELOPS

FACTORS responsible for the development of diabetic acidosis and coma are (1) failure to take insulin, (2) infection, and (3) combination of the two foregoing factors.

In Joslin's experience "the commonest cause of diabetic acidosis continues to be laxity of treatment, consisting of dietary indiscretions or neglect to take an adequate amount of insulin, or both." These factors were the cause of 53 per cent of a group of cases; infection was accountable for only 23 per cent. In my

CASE II							
Time	Insulin Units	BLOOD		Sugar	URINE Acetone	Diacetic	Therapy
		CO ₂	Sugar				
8:00 A.M.	25	19	325	4+	4+	4+	1,000 cc. 10% gm. in Sal.
8:30 A.M.	25			4+	4+	4+	400 cc. water
9:00 A.M.	25			4+	4+	4+	200 cc. orange juice
9:30 A.M.	25			4+	4+	4+	500 cc. N/6 lactate
10:00 A.M.	25			4+	4+	2+	200 cc. water
10:30 A.M.	25			4+	4+	0	200 cc. water
11:00 A.M.	25			4+	4+	0	1,000 cc. 10% gm. in Sal.
11:30 A.M.	25			4+	4+	0	400 cc. water
12:00 A.M.	25			4+	4+	0	200 cc. water
12:30 P.M.	25			4+	4+	0	200 cc. orange juice
1:00 P.M.	25			4+	4+	0	200 cc. water
1:30 P.M.	25			4+	4+	0	400 cc. water
2:00 P.M.	25			4+	4+	0	1,000 cc. 10% gm. in Sal.
2:30 P.M.	25			4+	3+	0	100 cc. orange juice
3:00 P.M.	25			4+	3+	0	200 cc. water
3:30 P.M.	25			4+	2+	0	200 cc. water
4:00 P.M.	25			4+	±	0	100 cc. grape juice
5:00 P.M.	25			4+	0	0	500 cc. 10% gm. in Sal.
6:00 P.M.	25			4+	0	0	200 cc. water
7:00 P.M.	25						

Patient was taking R20-0-P25; was well until a month before admission when he began losing weight, along with polyuria and loss of appetite. He became nauseated three days before and did not take insulin. For two days before admission he vomited all food, became drowsy and when admitted vomited a small quantity of blood.

P.E. P120 R40 BP. 105/50 T37

Semi-stuporous, Kussmaul. acetone in breath, eyeballs soft. Pharynx red. HBO 16: RBC 5.1: WBC 29,800: BUN 86. Acetone free in 9 hours.

experience infection and omission of insulin were the commonest causes for the precipitation of keto-acidosis and coma. The dietary breaks were not as impressive; after an analysis of 27 of our cases who did not adhere to a diet, we found that only 2 were eating more, while 25 ate less than their prescription called for. In a group of 220 cases of diabetic acidosis and coma, Bearwood and Rouse⁷ state that only 9 can be listed as breaking diet.

Although there is a difference of opinion concerning the breaking of diet as a factor in the development of diabetic keto-acidosis, it can be categorically stated that the most important cause is the omission of insulin, or a relative insufficiency of it, since during an infection its efficacy is considerably reduced. Consequently, a quantity which may have been sufficient during health to maintain the urine free from ketones becomes inadequate during an infection, and ketosis ensues.

HOW KETO-ACIDOSIS DEVELOPS

AT THIS point it is of interest to note how the diabetic develops keto-acidosis and coma. As you know, the overabundance of acetone bodies—acetone, diacetic, and betahydroxybutyric acids—in the blood and tissues causes an acidosis. This is brought about by a depletion of base. It was once thought that these acetone bodies were abnormal end products of fat metabolism. This hypothesis is not tenable today.

The experimental studies of many investigators have established the following facts. (1) Ketone bodies are normal intermediates of fatty acid catabolism in the liver—the only organ which manufactures them in significant quantities. (2) Ketone bodies so made in the liver are secreted into the blood stream where they are utilized by the peripheral tissues. This occurs both in normal and diabetic subjects whether or not insulin or carbohydrate is available. (3) Ketone bodies will not cause acidosis as long as their production does not exceed their utilization. However, when they are produced at a greater rate than they can be utilized by muscle and other tissues, they must of neces-

sity accumulate; it is this accumulation—resulting from overproduction—in the blood and tissues that starts the vicious cycle of acidosis, depletion of base, dehydration, and coma.

Why does the liver overproduce these ketone bodies? The obvious reply is that the liver is using for its energy the substance from which these bodies are derived, namely, fatty acids. Stadie's³ experimental studies led him to the conclusion that when the demand for fat calories exceeds about 2.5 gm. per kilogram per day, the production of ketones exceeds utilization, thereby producing ketonuria, and, if unchecked, leads to keto-acidosis and coma.

How can we prevent the liver from subsisting on fatty acids? By making carbohydrate available as liver glycogen. Liver glycogen has been termed the greatest factor of safety against ketogenesis. Here the hypothesis has been proposed by Mirsky,⁴ and indeed supported by fine experimental evidence, that a decrease of liver glycogen is the most likely stimulus to ketone formation. This is quite logical, for as the available carbohydrate is lowered, the liver will metabolize protein and fat. And as the combustion of fat reaches the figure of 2.5 gm. per kilogram per day as postulated by Stadie, the production of ketones will be accelerated to a point surpassing utilization with a sequential ketosis.

If, therefore, the liver is offered carbohydrate (glycogen) instead of fat, will ketogenesis be decreased? Evidence answers this query rather conclusively. A rapid drop in ketonemia and ketonuria was observed by Mirsky⁴ in depancreatized dogs after the administration of glucose intravenously. Root and Carpenter⁵ also reported a drop in blood acetone from 70 to 44 mg. in a diabetic patient three hours after 50 gm. of glucose were given by vein. It is obvious that glucose alone can decrease acetone formation both in the diabetic animal and patient, but to suppress ketogenesis insulin is also needed, since it has been shown that, when insulin is also used, the glycogen content of the diabetic liver increases more markedly⁶, and that the glucose so stored is not as rapidly dissipated. Thus, the liver is offered carbohy-

drate rather than fat for its own metabolic needs.

From the foregoing it is obvious that the diabetic will develop ketosis and coma if the liver catabolizes fatty acids in abnormal quantities. The liver will do this if glycogen is not available for its energy requirements. And, in the diabetic, the reduced glycogen stores are further lowered by omission of insulin, infection, or any other condition which reduces the potency of insulin.

METHODS OF TREATMENT

EACH group that has developed and employed a technique for treating diabetic acidosis insists that all the steps of its particular treatment are based on sound physiologic grounds. Mortality statistics are produced to support the thesis that such treatment is most satisfactory and, as additional support, explanations are offered on why the death rate is higher elsewhere. Such comparative data are neither satisfactory nor valid because of the numerous factors which determine the prognosis in each case. It is generally agreed that the results are dependent on (1) the duration of unconsciousness, (2) the age of the patient, and (3) the presence of serious medical complications.

If similar cases could be treated by the various methods, the superiority of one method over another might be determined. However, such an ideally controlled clinical experiment is almost beyond hope. Owens¹ has stated that even the so-called "best therapy" in the unconscious diabetic is highly unsatisfactory, while the duration of acidosis without unconsciousness is of considerably less importance. All agree that for the best results early treatment is imperative.

The most frequently employed measures in the treatment of diabetic acidosis and coma are (1) insulin, (2) fluids and salt, (3) blood analysis, (4) glucose, and (5) adjuvants—that is, N/6 molar lactate, transfusions, alkalis, lavage, enemas, and stimulants.

Everyone agrees that insulin is most urgently needed, since diabetic acidosis and coma are the end results of a relative or absolute insulin

insufficiency. Everyone, therefore, prescribes insulin—the difference is a quantitative one. The dosage recommended by various workers has varied from 25 to 400 units as the initial dose. Whenever the smaller doses are given, they are repeated at one-half hour to hourly intervals until improvement, as judged by clinical and laboratory data, is apparent. Olmstead⁷ gives 100 units at once and if there is no drop in the blood sugar after one and one-half hours, another 100 units is given. Joslin's group of 141 cases received an average of 206 units during the first three hours. There are still other variations, and the fact that good to excellent results have been obtained by all methods suggests that insulin is important, but that one dose or its frequency of administration is not superior to another dose given more or less frequently.

We have given 25 units—a small dose—at frequent intervals of 30 minutes. This plan, though empirical, has been satisfactory. That does not mean that giving 50, 75, or 100 units is not good therapy, even though the outcome in a series of cases may be poor. Owens¹ used 50 units of insulin every half hour at the start, and then altered the dose as indicated by progress. He also used all adjuvants, but reports a high mortality. Of 92 patients admitted, 49 were unconscious with an average of sixteen hours of coma. Among this group of 49 there was a death rate of 73.5 per cent. Does that mean that Owens's technique is inferior to ours, or that some one bungled the therapy? Not at all. His work is done in a general hospital with an active ambulance service, and he is called upon to treat more severe and more neglected cases than we do.

I decry the statement that some one has blundered if death occurs as a result of diabetic acidosis or coma. Many cases die in spite of generally accepted "superior" therapy, and no satisfactory explanation can be offered as to why death occurred. Schechter, Weisel, and Cohn⁸ suggest that peripheral vascular failure causes such deaths. Danowski, Winkler, and Peters⁹ state that the profound loss of salt and water may be the causal factors of such failure.

These hypotheses may be tenable as the patient in ketosis with shock has a decreased blood volume, a hemoconcentration, a hypochloremia, and a falling blood pressure. That may be the picture terminally. However, I have observed comatose diabetics whose blood pressure was maintained, whose chemical picture was corrected, and in whom no clinical evidence of peripheral failure was apparent. The therapy was considered adequate and yet such patients never regained consciousness.

The use of salt and fluids to replace the loss of base and water is so universal that no comment is needed. Often sixth-molar lactate was also used and transfusions were given only as indicated. We do not rely upon either the level of the blood sugar or the carbon dioxide combining power as guides of treatment. In our hospital and probably in others the results of the blood examination may not be available for one to three hours, at which time the data are of academic interest. Our principal laboratory guide is the examination of the urine for sugar and acetone at one-half hourly intervals, and we continue the insulin dosage of 25 units as long as acetone is present. The test is reliable and rapid, and therefore very practical.

THE question of whether or not glucose should be used in treatment of diabetic acidosis and coma has been argued with much passion and emotion. Many statements concerning the deleterious effects of glucose have been based on circumstances that were merely fortuitous. Our experience with glucose has not been unfavorable. As I have indicated above

we have used it as a 5 per cent and occasionally a 10 per cent solution intravenously. The median given in a twenty-four hour period was 112 gm. When the amount given by mouth was added to that, the median amount rose to a total of 312 gm. for the first 24 hours, with a minimum of 50 gm. and a maximum of 800 gm.¹⁰

Now it has been stated by Root¹¹ and his associates¹² that glucose in doses of 50 or more grams is harmful because (1) it obscures the actual blood sugar values thus eliminating a guide for insulin dosage; (2) it may produce liver damage; (3) it neutralizes the action of insulin; (4) the hyperglycemia thus produced is harmful to the pancreas; and (5) it may provoke anuria. It is also stated that such large doses are not necessary since the body can only metabolize 5 to 10 gm. per hour. These statements are made by respected leaders in the field with such conviction that the physician whose opportunity to treat diabetic acidosis is limited accepts them as facts. It is desirable to appraise them and see what evidence is available to support them.

That the administration of glucose obscures the actual blood sugar is a *fact*, and I have no objection if one wishes to use the blood sugar as a therapeutic guide. I maintain, however, that it is the excessive ketonemia, not the hyperglycemia, that is the underlying cause of diabetic acidosis and coma, and that therefore the ketone bodies in the urine are more accurate guides of therapy. Insulin should be continued frequently until the ketone bodies

TABLE A

Date	Fluid Intake	Urine Output	Glucose Gm./24 Hrs.	Urea N.	BLOOD			Serum P.	Icteric Index
					Sugar	CO ₂	Chlorides		
2/11	6350	170	870	65	223	62	479	4.4	—
2/12	2700	73	490	65	133	60	469	5.3	5
2/13	3795	21	760	69	190	49	446	5.5	—
2/14	2360	30	300	73	85	57	429	5.3	11
2/15	3930	47	700	85	89	51	423	5.7	—
2/16	3900	37	400	—	—	—	—	—	—
2/17	2800	105	300	—	—	—	—	—	—
2/18	4970	168	425	89	77	45	399	4.8	5
2/19	3815	908	400	100	79	41	376	—	—
2/20	3885	1930	300	104	—	40	385	5.0	—
2/21	4130	3150	500	111	85	40	396	5.1	—
2/22	4200	3850	500	102	—	45	421	—	—
2/23	0	4200	400	96	—	37	424	5.4	—

vanish; then there is no problem if one wishes to treat the hyperglycemia.

Astwood, Flynn, and Krayner¹³ have shown that liver damage occurred in dogs receiving glucose by vein at the rate exceeding 40 gm. per square meter per hour. They also demonstrated that dogs tolerated indefinitely 12 gm. per square meter per hour. These experiments have been offered as evidence that glucose may produce liver damage. Such reasoning is fallacious. Excessive quantities of any innocuous agent, even water, will prove toxic, and the fact that a dog may not be able to tolerate large quantities of glucose does not necessarily indicate that man cannot.

Recently, we had an opportunity to observe a patient in whom large quantities of glucose were not hepatotoxic. Following transfusion, a young woman developed a kidney shutdown. To facilitate diuresis large quantities of glucose were given by vein. Data are shown in Table A. This patient received from 300 to 870 gm. of glucose daily by vein. There was no glycosuria. Most of her blood sugars were normal, and one is led to the conclusion that the glucose so given was metabolized at a rate of 12.5 to 36 gm. per hour. Histologically, the liver showed no abnormalities.

Rabinowitch, Fowler, and Bensley¹⁴ have shown that the diabetic with the aid of insulin can also utilize more than 5 to 10 gm. of glucose per hour, as illustrated in Table B which follows:

TABLE B

Hours	32	48	43
Glucose Intake	1020	780	835
Excreted	10	32	63
Utilized	1010	748	772
Gm./Hour	31.5	15.5	18.0

It is true that Root and Carpenter⁵ used a different approach in determining how much glucose was metabolized. However, other data as well as ours are clear. It is obvious that if in my patient the glucose was not excreted it must have been used by the body.

The "neutralization" of the insulin by glucose is questionable. Perhaps, that is not what was meant, but the choice of the word "neutralize" was not the most desirable one. The

interaction of insulin and glucose is not the same as the neutralization of an acid by an alkali. Insulin favors the accumulation of glycogen, but its mode of action is not yet understood. Its action has been compared to an enzyme substrate reaction; and whether or not an excess of glucose is present, a certain amount will be acted upon by the quantity of insulin available. The beneficial effect of the insulin is not nullified by the excessive amounts of glucose.

Insofar as excessive quantities of glucose being harmful to the pancreas in the treatment of diabetic acidosis and coma, that is highly speculative. My own observations on post-mortem material failed to reveal histological changes in the pancreas in many instances. This is not an unusual observation, as Root also quotes two fatal cases which were treated with glucose in addition to insulin and whose blood sugars were 475 and 667 mg. per cent, and yet the autopsies were negative. It seems to me that there is altogether too much condemnation of glucose in the treatment of diabetic acidosis and coma. This indictment is not based on sound evidence.

I doubt whether the use or non-use of glucose is the crucial issue. I am sure that "suitable" cases will recover both with and without the use of glucose as long as adequate doses of *insulin, salt, and fluids are used*. The patient who has had a long period of unconsciousness will probably die in spite of the so-called "very best" treatment. Personally, I have had good results with frequent small doses of insulin and the use of glucose. The addition of glucose gives me the added feeling of security that I will not throw my patients into the hypoglycemia phase thus putting an additional burden upon a circulatory system already under considerable stress.

SUMMARY

1. Patients with diabetic acidosis, diabetic coma, or both can be successfully treated by giving small and frequently repeated doses of regular insulin—25 units every half hour—by replacement of water, and by giving salt and glucose by mouth, vein, or both.

2. The administration of glucose by vein or orally is beneficial and not harmful. Data are presented to support this thesis.

3. It is unnecessary to follow the blood sugar or the carbon dioxide combining power as guides of therapy. Our experience has shown that the clinical response and the disappearance

of the ketone bodies are excellent guides.

4. The earlier the treatment is begun, the more favorable is the prognosis. Exclusive of medical complications, it can be stated categorically that the longer the patient remains unconscious, the less favorable are his chances for recovery.

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MONGOLISM

The diagnosis of mongolism not infrequently is made by parents who after a long period of emotional attachment realize that their child is not "right." Cummins and Platou point out that this brutal accident may be avoided if the physician has better knowledge of the stigmata associated with this deformity. These investigators selected three characteristics which occurred most consistently in known mongoloid idiots and compared the diagnosis, using these criteria with those obtained clinically. The criteria are: (1) a distinctly transverse alignment of skin ridges in the distal region of the palm; (2) a patterning of ridges in the hypothelar area, forming an arch, whorl, or loop; and (3) a triradiate arrangement of ridges at or near the center of the palm. The two latter characteristics are associated.

Prints from 86 persons were analyzed by dermatoglyphic studies. Forty-nine clinically certain mongoloid idiots were diagnosed correctly, as were twenty-seven normal controls. Of the remaining ten, unequivocal disagreement occurred four times and partial disagreement three times. The clinical diagnosis itself was uncertain in three cases. Hence the palmar stigmata yielded diagnoses as accurate as clinical diagnoses in seventy-six out of eighty-three patients.

Ideal Stumps and Prosthetics for Amputees

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SUCCESS in amputation surgery is achieved only after prosthetic fitting has been completed and the patient has been rehabilitated. Prosthetic fitting requires the coordinated efforts of the surgeon and the limb-fitter. The latter has a preference for certain classical levels of amputation because of ease of fitting and because standard devices have been made to fit these stumps. This preference has sometimes led to reamputation at higher levels in order to obtain what is considered an ideal stump. In actual practice, reamputations should be performed only for surgical indications such as infection, scar tissue, and circulatory disturbance. As a rule, a stump in excellent functional condition should have a prosthesis fitted to it rather than have the stump revised to fit a particular type of prosthesis. Many cases with wrist disarticulation, short below-elbow stumps, short below-knee stumps, and knee disarticulation have been functionally superior to higher levels because the length and contour of the stump has provided control of the prosthesis which was not otherwise possible. With increasing improvement in prostheses and with diligent effort, these cases can be well fitted.

As much of the extremity as possible should

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be saved at the time of an open amputation. Likewise, in a definitive amputation or revision, as much length as possible should be conserved, observing the necessity for good soft tissue coverage and a clean, healthy stump. The one exception to this rule is in the area between the level of a Syme amputation and the mid-leg. The long leg stump is not as desirable as amputation at or above the middle of the leg. With this possible exception amputation is seldom justified at a higher level than otherwise necessary in order to facilitate fitting.



Leonard T. Peterson

The amputation stump should assume its function of propelling a prosthesis as soon as possible after amputation in order to toughen weight-bearing points, to develop muscle power, and to preserve joint motion. A prosthesis can ordinarily be fitted about six weeks after amputation or revision if primary healing occurs. The early use of a prosthesis toughens the stump to a firm, healthy condition free from edema or excess tissue. If fitting and training are unnecessarily delayed, the amputee adapts himself to the handicap of the loss of a limb and he is not likely to become proficient in the use of a prosthesis.

THE stump is prepared for a prosthesis by firm bandaging with an elastic type of bandage, which is applied daily or oftener and which should be anchored above the next joint, especially if the stump is short. Active exercises are practiced with increasing resistance in order to develop weak muscles that are essential for proper use of a prosthesis, such as the deltoid, gluteus maximus, thigh adductors, and quadriceps. It is especially important to prevent joint deformity during convalescence. The use of massage has largely been abandoned in favor of bandaging, exercise, and early fitting.

The stump undergoes shrinking after fitting, so that the socket is soon too large and refitting is required. The longer the period of preparation before fitting, the less change will occur subsequently. However, the use of a prosthesis is by far the best method of shrinking and training the stump. Less change occurs in the upper extremity than in the lower, and the first prosthesis may be the permanent one. In the case of the lower extremity, however, repeated fitting is necessary during the first year. A lack of limb-fitting facilities or economic conditions may require the use of a temporary plaster pylon or temporary leg. A provisional leg with a standard design and adjustable features facilitates the fitting of a large number of amputees, especially in wartime. If adequate materials, skilled labor, or cost need not be considered, the same objective can be attained

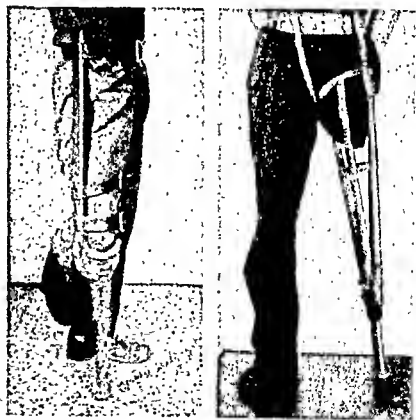
by the replacement of at least the socket of the permanent prosthesis as occasion demands.

The early training and fitting of the amputee requires close cooperation between the surgeon, limb-maker, physical and occupational therapists, and the patient. The program should be closely supervised by the surgeon responsible for the case.

LOWER EXTREMITY

Mechanism—A pylon is quite satisfactory for a Syme or below-knee stump, but it is an *undesirable* substitute for a provisional or permanent limb in the case of an above-knee amputation stump. The importance of a knee joint with friction control and of a carefully fitted hip control in developing proper walking habits make it desirable that these features be provided the above-knee amputee as early as possible. Pylons will, however, be useful where geographical or economic conditions require their use beyond the early postoperative period. (Figures 1 and 2.)

The knee joint for the thigh amputee should have stability on weight-bearing, ease of control, and durability. Some knee joints are made



Figures 1 and 2. Pylon for a Syme or above-knee stump.

to resemble the normal action of the human knee. Stability on weight-bearing (Figure 3) is important for the new amputee because if the knee buckles he falls down. The ideal knee would lock automatically on pressure at various degrees of flexion and still not interfere with normal activities such as sitting or descending stairs. Advances are being made in the use of new methods of hydraulic and mechanical control. Simplicity, durability, and ease of repair and replacement should be considered in the selection of the proper mechanism, but these factors should not prevent the progressive use of new and improved devices.

Hip control and harness—Formerly, the above-knee prosthesis was secured to the body by a shoulder harness which is still in use in some countries and by some of the older amputees in this country. The shoulder harness fails to give firm control of the prosthesis. A

more important objection to the harness is the faulty gait which develops since the amputee lifts the prosthesis by raising the shoulder of the same side much higher than the other while he tends to come up on the toes of the normal foot. This shoulder-hunching gait is very conspicuous and undesirable. A harness may be required in addition to a hip belt, especially in the bilateral case, but its use has otherwise been abandoned in favor of the metal hip control.

Deformity—If a stump has flexion or abduction contracture, the socket must be fitted in the relaxed position of deformity, and then the rest of the prosthesis is fitted to compensate for the deformity. Deformities must be corrected before fitting, or they must be fitted as deformed. The prosthesis does not correct a deformity.

THE usual deformity in the below-knee stump is a flexion contracture of the knee joint so the joint cannot be completely extended. The socket must be made to fit the long axis of the stump and the axis of the leg below this level changed to align it properly for weight-bearing. Some fitters fit the below-knee stump in very slight flexion as a method of choice. A stump that has 45° flexion contracture can be fitted satisfactorily in this manner, preserving the remaining knee motion for flexion and extension of the prosthesis. Very short flexed stumps can be fitted with a "bent knee" prosthesis, in which the patient kneels in the socket, which is shaped posteriorly to accommodate the end of the stump. This makes an excellent end-bearing or true knee-bearing prosthesis which is functionally superior to an amputation at a higher level.

An amputation through the thigh is ordinarily fitted with an ischial-bearing prosthesis so that the amputee sits on the socket, bearing his weight on the ischial tuberosity. If the amputation is at or above the level of the perineum it requires a "tilting table" type of prosthesis in which the socket fits the hemipelvis and the prosthesis is propelled by a

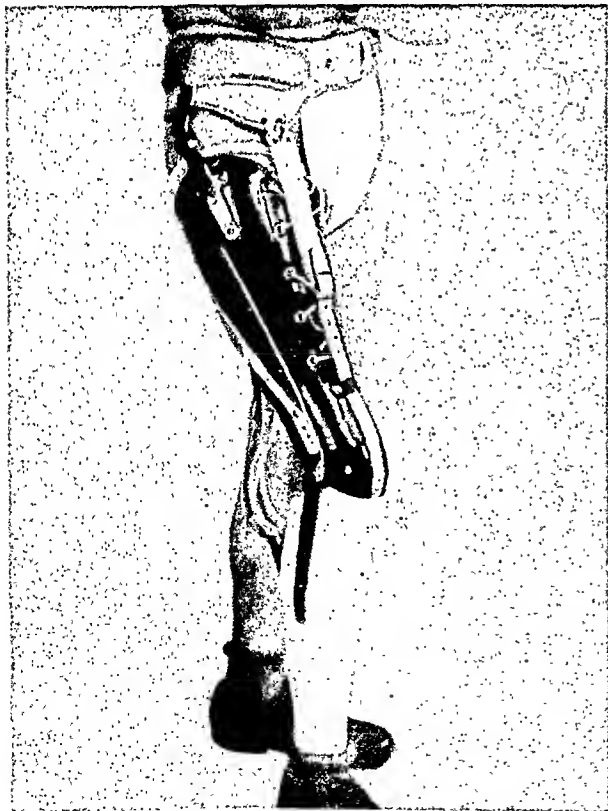


Figure 3: Knee joint for thigh amputee—should have stability on weight bearing, ease of control and durability.

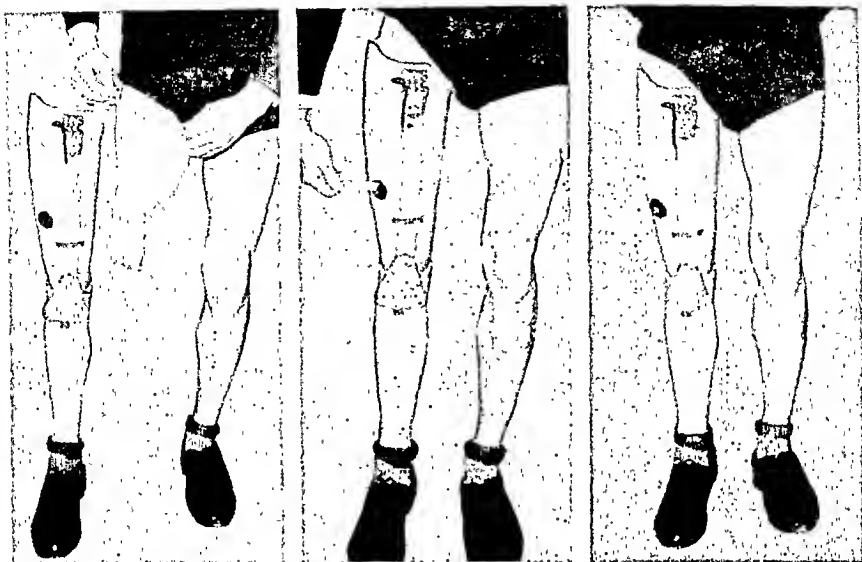


Figure 4: The stump is inserted with a thin stump sock which is then pulled out through the valvo opening, thereby pulling the stump down firmly in the socket (figure 5) before the valve is closed (figure 6).

pendulum action, since there is actually no stump to propel it.

The end-bearing thigh stump resulting from amputation through the lower end of the femur should be fitted with an end-bearing socket, unless there is some contraindication to weight-bearing at this point. Some manufacturers prefer to make the ischial-bearing socket rather than build a proper end-bearing prosthesis because the long stump interferes with the standard knee control.

From the prosthetic standpoint, knee joint disarticulation has not been popular in the past. Amputation at this level is not common because below-knee or end-bearing above-knee (transcondylar) levels are preferred for fitting. However, a knee disarticulation which is covered by good skin can be fitted on the same principles as the other end-bearing or bent-knee stumps, and the level alone does not

indicate reamputation. A properly fitted knee disarticulation is an excellent functional stump. To date, the end-bearing stumps have had to be fitted without the friction knee control desired in above-knee prosthesis, because a suitable mechanism has not been available. No doubt this will be available for end-bearing prostheses in the near future. In the meantime the advantages of a good end-bearing stump should not be sacrificed for the sake of fitting a knee control.

The suction socket—The suction socket is widely used for above-knee amputees in Germany but has had little application elsewhere. The socket is accurately fitted to the stump and provides ischial weight-bearing as described previously. Below the end of the stump the socket has a valve which permits air to escape when the stump is inserted. Then on closing

the valve the socket is airtight so that lifting the stump or pulling on the leg tends to produce a suction effect due to the force of atmospheric pressure. The stump is inserted with a thin stump sock which is then pulled out through the valve opening, thereby pulling the stump down firmly in the socket before the valve is closed. If the socket is properly fitted and the stump is in good condition, it gives the amputee firm control of his leg without the use of a pelvic belt and, in fact, the prosthesis cannot be pulled off manually without opening the valve. Only the short stumps, four to five inches in length, use any support, consisting of a harness or belt. The skin is in contact with the socket without any intervening sock, but there is no ill effect if the socket is properly finished. Stumps that are imperfect surgically may suffer edema and ulceration as in the case of conventional sockets. The satisfaction expressed by users of suction sockets indicates that this method of fitting deserves more attention than it has received heretofore. (Figures 4, 5, and 6.)

THE below-knee (B-K) prosthesis is used for all below-knee stumps between the level of the knee-bearing and the Syme stump. If the stump is in good condition and has undergone proper shrinkage and training, all the weight can be borne on the socket. The thigh corset gives some support, but its purpose is not to bear the weight (Figure 7) by tight lacing since this interferes with circulation of the stump and produces atrophy of the thigh. In below-knee stumps that cannot tolerate full weight-bearing, the stump has great value in controlling and propelling the prosthesis. In these cases the stump can be protected for a long period of usefulness by fitting a molded ischial-bearing thigh corset so that all or most of the weight is borne on the ischium while the leg stump is used only for control.

The Syme amputation is performed through the tibia and fibula immediately above the articular surface of the ankle. The end of the

stump is covered by the heel skin which must be in good condition for weight-bearing. The Syme stump bears all the weight on the end and is fitted with a prosthesis that does not extend above the knee. The Syme amputation is the best and most serviceable stump in the lower extremity. It is, however, not suitable for women for cosmetic reasons because the ankle region is bulbous and conspicuous.

Fitting and training of the amputee—The proper fitting of the amputee is the responsibility of the limb-maker. The great importance



Figure 7: The thigh corset gives some support but its purpose is not to bear the weight by extremely tight lacing since this interferes with circulation of stump and produces atrophy of thigh.

of proper fitting has unfortunately overshadowed the equal importance of better materials and of mechanisms of improved quality and design. The basic principles of fitting are well established, but as new developments are made in material and design, new techniques of fabrication and fitting must follow. For

successful use of a prosthesis the socket must fit the stump without causing pain or constriction. In the case of the thigh stump the socket should fit snugly on the lateral surfaces while the ischial seat takes the body weight on the tuberosity of the ischium. Proper weight-bearing can be tested by inserting the finger between the ischium and the socket. When the body weight is applied, it will normally rest on the finger. Pressure must be relieved from the perineum without causing the tissues to roll over the edge of the socket since painful pressure in this region will cause the amputee to walk with a widely abducted and awkward gait. If the socket is too large after application of three stump socks, it should be replaced or be lined.

The below-knee stump is the most difficult to fit because weight is taken on a relatively small surface area and on tissues not accustomed to bear weight. Painful areas must be relieved of pressure while the weight is equally distributed over the remaining surfaces of the stump and the thigh cuff. The back of the socket should provide space for the hamstring tendons but should come as high in the popliteal space as full knee flexion will permit, while anteriorly the socket comes to the inferior border of the patella. The socket must be longer than the stump and exert uniform pressure in order to prevent terminal edema. A properly fitted socket will fit the stump in only one position. Any change in rotation of the socket requires refitting in relation to the joints and the container that holds it. The hip, knee, and ankle joints must be properly aligned to enable the amputee to walk with a smooth gait in which there is no abduction or rotary motion of the prosthesis. It should not be necessary to twist the pelvis into any abnormal position to permit direct forward propulsion of the limb.

THE length of the prosthesis should correspond to the normal extremity. No exception should be made to this rule in the below-knee or long thigh stump. Short thigh

or hip stumps may require one half to one inch shortening to facilitate the pendulum action without raising the pelvis on that side.

Instruction in the use of a prosthesis—The amputee should receive training by qualified instructors as soon as he is fitted with the prosthesis. Special facilities are desirable in physical therapy, especially for the lower extremity amputee, and in occupational therapy, especially for the upper extremity amputee. It is recommended that at first the prosthesis be worn for only a short period daily so that the stump may become gradually adjusted to the socket. Excessive use early will cause the stump to become irritated and painful. When the leg is removed, the stump should be firmly bandaged with an elastic bandage or swelling will occur and the stump will be too large the following day. The prosthesis should be kept in the clinic and worn only under supervision until the amputee becomes proficient enough to use it independently without developing faulty habits. The stump should be carefully examined for evidence of muscle weakness and imbalance and for evidence of joint contracture since muscular strength and normal joint motion are essential. The normal extremity and the spine should be flexible and the posture should be as nearly normal as possible.

Where a large number of amputees are undergoing training, they are best divided into sections according to the level of amputation. Special provision is made for bilateral and other unusual cases. The use of individual movies offers an excellent medium for training, since this gives the amputee an opportunity to analyze his own faulty habits and to observe his progress.

THE UPPER EXTREMITY

The hand mechanism—A hand may be of a mechanical or cosmetic type. Mechanical hands lack a satisfactory cosmetic appearance and require a glove for covering which makes them conspicuous in the summer when gloves are not worn. Mechanical hands, unfortunately, have also lacked functional value and have been heavy. Hands have been made of wood,

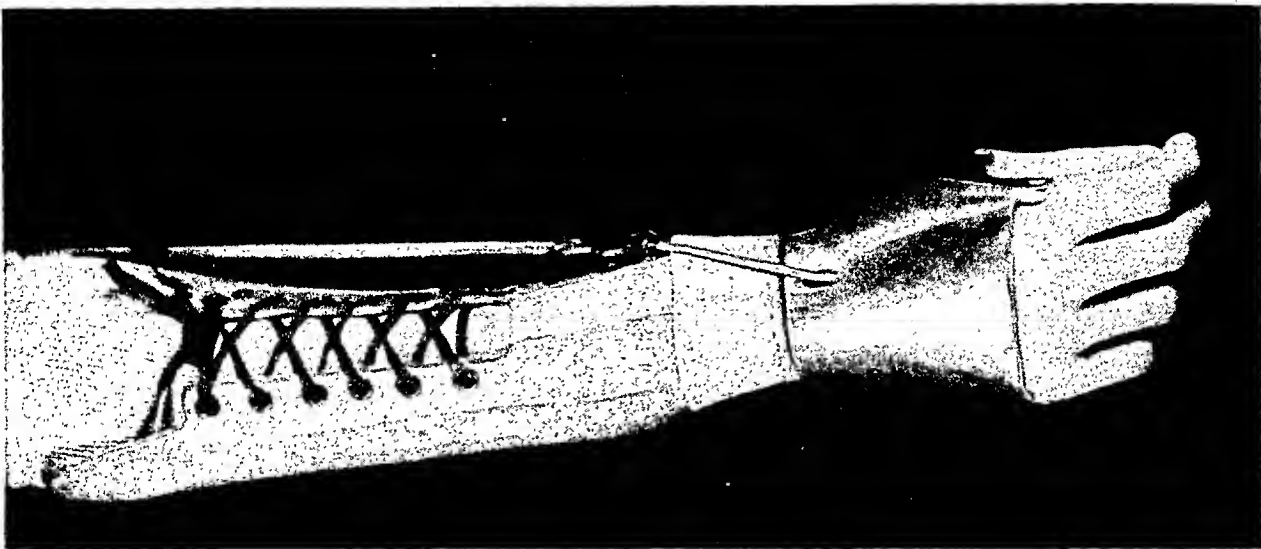


Figure 8: Hand (Miracle), made with an aluminum palm, rubber thumb and fingers, articulated at the metacarpal phalangeal joints; provides active closing and passive opening.

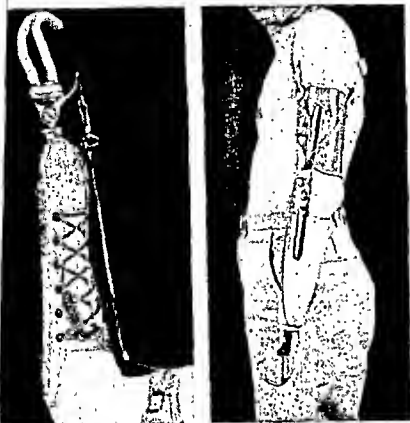
metal, rubber, or a combination of metal and rubber. Wooden hands are usually articulated in the thumb alone or in the thumb and fingers at the metacarpal phalangeal joint and are opened by action of the cord, closing passively by spring action. One type of hand (Becker) contains thumb and fingers of coiled wire with rubber finger tips all activated in that way. (Figure 8). The miracle hand, which is made with an aluminum palm and rubber thumb and fingers, articulated at the metacarpal phalangeal joints, provides active closing and passive opening which is more desirable since closing the hand is normally a more important and delicate motion than opening. Only the double motor cineplastic prostheses described below provide both active flexion and extension of the fingers and thumb.

Until recently no serious attempt has been made to construct a cosmetic hand. Now, however, good cosmetic hands are being made of rubber and of plastic materials. These match the normal hand, but durability of the color and material is still limited. The cosmetic hands have not had any functional value and few experimental attempts have been made to combine mechanical and cosmetic features in the same hand. Replacing the human hand

with an artificial one presents a problem much more difficult than replacing a leg because the latter is relatively simple and less conspicuous. Until recently research in this field has not kept pace with modern industry. While improved devices are now being produced, they are still in the laboratory stage and further developments, improved manufacturing, and new fitting methods are still required.

The hook—Mechanical hooks (Figures 9 and 10) have great utility value for the amputee and are essential for the bilateral case. A hook is very conspicuous and objectionable to many amputees, but its functional value makes it desirable that all cases be trained in its use early during convalescence. The hook can readily be interchanged with a cosmetic hand for dress purposes.

VARIOUS hooks have been designed but they may be classed as rigid and split types. Of the latter, the Dorrance type is the most popular. Split hooks are almost unknown in Continental Europe, though used extensively together with other mechanical tools in this country and in Great Britain. The hand or



Figures 9 and 10: Mechanical hooks have great utility value for the amputee and are essential for the bilateral case.

hook is activated by a cord attached to the harness around the opposite shoulder, except in case of the cineplastic amputation. An improved cord designed by Northrop Aircraft, Inc., consists of a multiple-strand wire cable contained in a flexible metal housing. It readily transmits force around the curves without serious mechanical interference. Pneumatic, hydraulic, and electrical methods of control have not had practical application to date.

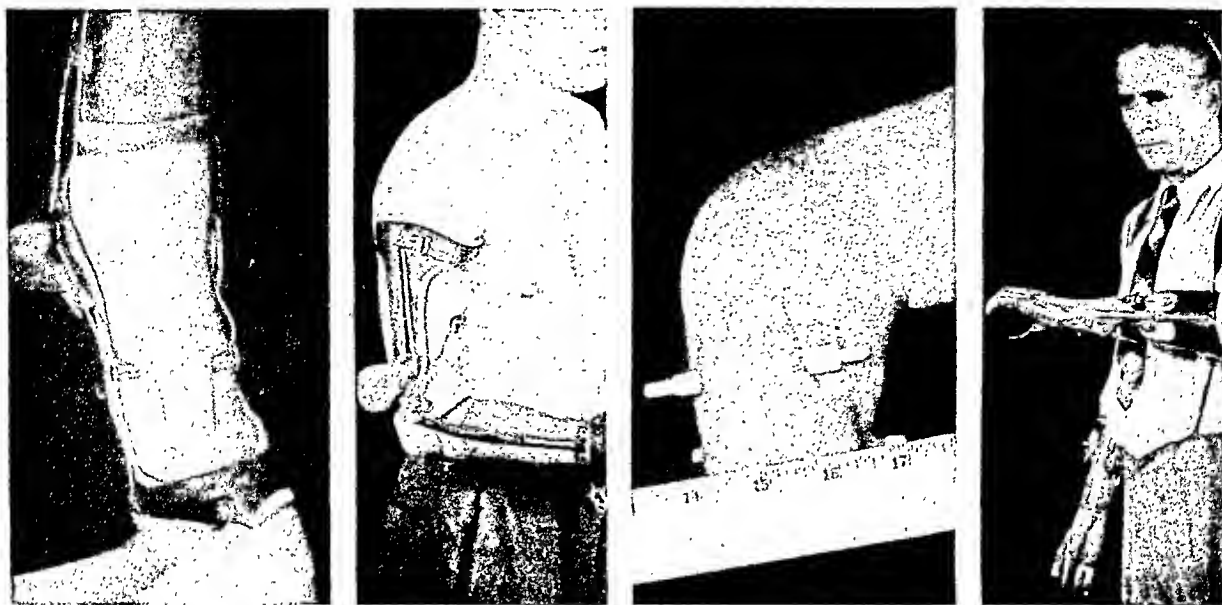
The wrist mechanism—The best wrist mechanism at this time for the forearm stump is a lightweight metal rotary wrist designed by Northrop Aircraft, Inc. This device is useful in case of amputation through the middle or distal third of the forearm. It requires a double plastic socket; the inner or true socket fits the stump and is attached to the driving mechanism of the wrist, which rotates within a metal casing; this, in turn, is attached to the outer section of the forearm. A system of locking rollers in the wrist, controlled only from the proximal end, prevents rotation from the hook end but permits the stump to control the rotation with ease. The mechanism can be adjusted to lock as above or the locking rollers can be

removed if desired. The unit can be made so that the hook will rotate through the same arc as the stump, or the ratio can be increased to nearly $2\frac{1}{2}$ to 1. Rotary wrists have previously been used in several types of above-elbow prosthesis by providing automatic rotation on elbow flexion.

The elbow mechanism—An improved metal elbow joint of lightweight and excellent construction has also recently been developed by Northrop Aircraft, Inc., for above-elbow amputees. This provides locking and unlocking in any position and is controlled by shrugging the shoulder. The mechanism is bonded to a plastic socket above and to a plastic forearm below.

Shoulder amputations—Interscapulo-thoracic or forequarter amputation leaves a marked asymmetry, since the sloping chest wall has no covering except skin and subcutaneous tissue. A complete prosthesis is not indicated because there is no stump to support the prosthesis. However, a light shoulder pad contoured to fit the body and to match the other shoulder will greatly improve the appearance. Amputation between the shoulder joint and the lower border of the pectoralis-major tendon leaves no stump of functional value in activating a prosthesis. However, a cosmetic arm with very limited functional value can be suspended by a socket fitted over the shoulder. This is made of molded leather or preferably light plastic material and held in place by straps around the chest and other shoulder. The rest of the prosthesis should be as light as possible. The hook can be operated from the opposite shoulder, but the amputee should not expect to find this prosthesis very useful. Many amputees have found that a prosthesis fitted at this level is more of a burden than a benefit.

Short arm stumps are better fitted with a short working prosthesis than with the conventional full-length type. The latter can be made detachable just below the socket so that a working tool can be inserted, thereby giving greater efficiency than if the tool is attached at the level of the wrist. The British have used



Figures 11, 12, 13, 14: Cineplastic amputation utilizing individual muscles or muscle groups to activate a prosthesis independent of the general movement of the stump itself. This is accomplished by the construction of motors, or skin-lined tunnels through the muscles, to which the prosthesis is attached.

this principle to greater advantage than others. For cases having an intact pectoralis major, a cineplastic motor through this muscle offers considerable benefit as a holding mechanism and as a source of power.

The arm stump—A minimum stump length two inches below the pectoralis major is desired for a satisfactory fitting. The socket is made of wood, aluminum, leather, or, preferably, plastic. The material should be strong, light in weight, and silent on contact with external objects. The actual choice between materials that meet these requirements is a matter of individual preference. A plaster mold of the stump is covered with two or more layers of stockinette impregnated with a thermosetting resin. The elbow assembly is aligned in the proper axis in relation to the stump and is incorporated in the lower end of the socket corresponding to the level of the normal elbow.

AMPUTATION through the condyles of the humerus leaves the end of the stump broad and flat. This level may make fitting more difficult because of a bulbous end, but

the contour of the stump enables the amputee to control the prosthesis much more effectively than in the case of a tapered stump. As in the case of the long thigh stump, the length here may interfere with fitting of a desirable joint assembly but the advantages of the long stump outweigh the advantages of a special mechanism.

The forearm stump—As much of the forearm as possible should be conserved for prosthetic fitting. The functional value of the stump is measured from the biceps tendon downward, but a stump at or above this level still has value in stabilizing and controlling the prosthesis. The functional length of the stump can be increased for fitting purposes, by cutting the biceps tendon leaving only the brachialis muscle for elbow flexion. However, the biceps should not be cut for the purpose of fitting if a biceps cineplastic motor is contemplated at a later date. The forearm socket is cut out of wood or is fashioned over a mold of the stump using aluminum, leather, or plastic. By various combinations of plastic materials the degree of hardness and resonance of the socket can be

controlled. If the rotary wrist is used, an inner socket and an outer container are required; the former is attached to the driving mechanism of the wrist, while the latter holds the outer casing and elbow joints.

Amputations through the carpal bones or wrist joint have in the past often been subject to reamputation at a higher level in order to obtain what was considered an ideal stump for fitting, since the longer stumps fitted by conventional methods tended to make the prosthesis longer than the normal side. However, it is recognized that the ability to rotate the finger stump without the use of a special mechanism is of great practical value. If the wrist stump is in good condition from the surgical standpoint, it can be fitted by a simple flexible or rigid leather or plastic socket. No retention cuff is necessary above the elbow, and a very simple harness is required to support the activating cord.

CINEPLASTIC AMPUTATIONS

A cineplastic amputation utilizes individual muscles or muscle groups to activate a prosthesis independent of the general movement of the stump itself. This is accomplished by the construction of motors, or skin-lined tunnels through the muscles, to which the prosthesis is attached. The practical application of this procedure has been limited to the upper extremity, and its success depends on proper surgical technique, muscle training, and the fitting of a satisfactory prosthesis (Figures 11, 12, 13, and 14).

Cineplastic surgery has received little attention outside Germany. Its use in the United States has been limited to the work of H. H. Kessler of Newark and Nissen and Bergmann of New York. Only one manufacturer in this country has supplied the prosthesis. At the end of World War II interest in this subject was again renewed because of the observation by American surgeons of the work of Lebsche in Munich. Lebsche has performed more than 500 cases, and his surgical technique and functional results merited special study. Therefore, a

War Department Commission, including the author and other representatives of the Surgeon General's Office and the Committee on Prosthetic Devices, visited Europe in March and April, 1946, for a study of amputations and prostheses including cineplastic methods. This Commission reported:

"CINEPLASTIC surgery at the pectoral, arm, and forearm levels has reached a high degree of perfection in Professor Lebsche's clinic in Munich. With proper attention to technical details and with careful postoperative training, excellent results can be obtained in properly selected cases. Meticulous surgery, the use of large skin tubes, and the liberation of the distal end of the muscle in all cases contributed to the superior results observed in his cases in comparison to those observed elsewhere. A number of cases which had been performed outside Munich or Berlin were unsatisfactory because of improperly placed tunnels, small tunnels, and necrosis of the skin. The wide range of excursion and the considerable strength in the better cases should prove of great value in further development of cineplastic prostheses."

The commission recommended as follows:

"1. That cineplastic surgery be approved for properly selected upper-extremity amputees according to the technique of Professor Lebsche. A number of carefully controlled cases should be performed in order to perfect the cineplastic prosthesis and to determine its value in this country.

"2. That the Krukenberg amputation be approved for properly selected bilateral upper-extremity amputees, with special application in the blind.

"3. That arrangements be made to obtain from Munich three or four cineplastic amputees of various types in order to demonstrate the value of the operation and in order to test redesigned prostheses. Similar cases could be produced in this country but the necessary surgery and postoperative training would delay the program at least six months.

Thiouracil, Thiobarbital, Propyl Thiouracil and the Treatment of Hyperthyroidism

FRANK H. LAHEY*

LAHEY CLINIC, BOSTON

THERE has been so much discussion, written and spoken, and considerable disagreement and confusion concerning the use of the thiourea group of drugs in the treatment and preparation of patients with hyperthyroidism for surgery that I thought you would like to hear about our practical experience with these drugs. I understand that you have had expressed to you some opinions of the value of thiouracil as a substitute for surgery, and I should like to present our views and the reasons why we differ. We feel very strongly, and I think there will be more and more evidence to indicate that thiouracil, thiobarbital, and propyl thiouracil are not to be safely used as substitutes for surgery.

I should also like to discuss another method of treating hyperthyroidism and to state our reasons for opposing it, namely, the use of irradiated iodine. The basis for using irradiated iodine in the treatment of hyperthyroidism is the fact that if a given dose of iodine is administered to a patient, of that iodine 80 per cent will be accepted by the thyroid gland. Therefore, the principle of the use of isotopes, as proposed by the Lawrences in Berkeley, such as the exposure of phosphorus in the cyclotron and the intravenous use of irradiated phos-

phorus, was transferred to the use of irradiated iodine in the treatment of hyperthyroidism.

How does the treatment work? It works literally by depositing 80 per cent of the irradiated iodine in the thyroid gland so that the radiation effect will be directly upon the thyroid gland and thus produce a depression of its activity. In simple terms, what it really does is literally to fry the thyroid. The deposit of radiation in thyroid cells results in a fixed, firm, hard state of thyroiditis in the thyroid gland which brings about varying degrees of inactivation and destruction.

We personally are opposed to a method which by hit or miss accomplishes destruction of thyroid tissue irrevocably. We believe in addition to this that since 20 per cent of the irradiated iodine is not accepted by the thyroid gland, its long-range results, particularly upon kidney tubules and possibly as a promoter of malignancy, have as yet not been settled. We believe that the long-range effects of the intense thyroiditis which results from the deposit of irradiated iodine in the thyroid and the cicatrization and later fibrosis and fixation which occur are as yet unproved in terms of possible later complications. We do not believe that a method which is as uncertain in its degree of destruction of thyroid activity, and certainly unproved and unseasoned in terms of its possible ultimate complications, can be compared with a surgical method, subtotal thyroidectomy, which we will submit to you has now, with the use of

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thiouracil, thiobarbital, and propyl thiouracil, had its mortality reduced to 0.17 per cent. It is about these three drugs that I wish to speak.

I should like to say now that we have abandoned thiouracil and thiobarbital entirely because they have such a high percentage of complications, and we now employ only propyl thiouracil. The incidence of disagreeable and dangerous complications from the administration of thiouracil is 9 per cent; the incidence of complications from the employment of thiobarbital is 28 per cent; and the incidence of complications from the employment of propyl thiouracil is 2 per cent (1 patient had a fever reaction; 5 patients had white cell depression, 1 of whom developed agranulocytosis) in 210 patients prepared for surgery and 90 more still under preparation. The incidence of complications of propyl thiouracil is so low that we have abandoned the other two drugs except under circumstances of which I shall speak.

The patient mortality in 25,000 operations for thyroid disease is 0.88 per cent and the operative mortality 0.75 per cent. Since the use of thiouracil in July, 1943, and now propyl thiouracil, mortality has dropped to 0.27 per cent, using one of these three drugs to prepare patients with hyperthyroidism for surgery, and in the last year it was 0.17 per cent, the one death being a case of thrombosis. In the first ten months of 1946 there have been no deaths, so that the present operative mortality figures in 670 patients with toxic goiter prepared for surgery is 1 death (coronary infarct).

I would like now to review quickly how these drugs act. We know that from the pituitary gland comes the stimulating hormone which produces hyperplasia in the thyroid gland. We do not, however, know how this group of thiourea drugs accomplishes its effect, which is to inhibit the synthesis of thyroxin completely even in the presence of a histologic appearance of the thyroid gland of hyperthyroidism, that is, hyperplasia. We know that the protein-bound iodine which represents the synthesized thyroxin diminishes hand in hand with the improvement in clinical symptoms and the basal metabolism. We know that the hyper-

plastic cell which characterizes the histologic appearance of hyperthyroidism persists in spite of the fact, as already stated, that the metabolism comes to normal, and this is of particular importance to the surgeon.

I have frequently said, after operating upon patients with hyperthyroidism who were prepared for surgery solely with thiouracil, never having had any iodine, that if I had to operate on patients so prepared, I would prefer to give up thiouracil. The reason I make this statement is that in patients prepared solely with thiouracil, as all surgeons know, the gland is still hyperplastic, bleeding is terrific, and the gland will not hold hemostats, double hooks, or ligatures, and it is next to impossible to control the bleeding and to do anatomical dissection.

We have devised and for the past two years have practiced the plan of combining iodine with the thiouracil, and now propyl thiouracil, to produce an involution that devascularizes the gland, compacts its epithelium, and makes conditions which are much more ideal for surgery.

IN THE beginning of our experience we stated that these patients should have thiouracil during the first of their period of preparation and only during the last three weeks of preparation should they have Lugol's solution. We have now changed that so that they now receive Lugol's solution and propyl thiouracil throughout their period of preparation. This has prolonged the period required to bring their metabolism to normal a little, but it has resulted in more prompt improvement in symptoms early in their preparation and complete involution and devascularization of the gland.

We have learned that the period of time taken to prepare these patients for surgery will vary in different types of thyroid glands. In patients with hyperthyroidism who have had the disease nine months or less and who have not taken iodine, there will be an average daily drop in metabolism of about 1.3 per cent. If iodine has been taken, the drop in metabolism will be at the rate of about 1 per cent per day. If the hyperthyroidism is over one year in du-

ration, irrespective of iodine, this drop will also be at the rate of about 1 per cent per day. In the patients with large, toxic adenomas, however, particularly in those who have had iodine, there will be a slower rate of drop in metabolism, approximately 0.5 per cent per day, and the longest time we have ever taken to get the elevated metabolism of a patient with a toxic adenoma to normal is 180 days.

In general, in exophthalmic goiter it can roughly be said that it will take the number of days to bring the metabolism to normal that it is above normal.

We have repeatedly been told by visitors that they are unable to bring the metabolism in these patients to normal. In our opinion, this is due to the fact that either they do not give enough of the agent or they do not give it long enough, or, still further, there may have been a complication, because in no case have we failed to bring the metabolism to normal when we have given it long enough.

I think there have been a good many misleading statements in the literature concerning these drugs, particularly propyl thiouracil. It has been stated that administration of propyl thiouracil does not result in any complications. That is not true. We have had 5 cases of white-cell depression, in 1 of which agranulocytosis developed, and 1 case of fever reaction. It is our opinion that if one uses large enough doses of propyl thiouracil to bring the metabolism to normal, that is 200 mg., there will be an occasional depression in the white and differential counts.

WE HAVE frequently been asked, "How often must white and differential counts be done?" Probably the safe period is approximately once a week or once in ten days. We have often also been asked, "At what period should one cease administering these agents as relates to the white count?" When the white count has fallen as low as 4,500 and when the granulocytes are found to be reduced to 45 per cent, further administration of these agents should be discontinued and the patient should be carefully watched for further drop.



Frank H. Lahey

One other thing to be noted is that in the preparation of patients with propyl thiouracil for surgery, no propyl thiouracil is given for the last week. The reason is that we have seen agranulocytosis appear one week after the last dose of the drug has been administered, and we do not wish to have to deal with the complication of an agranulocytosis which comes at the time of the operation or during the period immediately afterward.

Multiple-stage operations have disappeared in the last three years during which time we have employed this drug. The mortality has progressively dropped to 0.17 per cent. We have recently reported our experiences with 25,000 thyroid operations upon 22,000 patients. The operative mortality in the 25,000 operations was 0.75 per cent and the patient mortality 0.88 per cent. During the last three years since we have been preparing these patients for surgery with one of these three agents, thiouracil, thiobarbital, or propyl thiouracil, the mortality has dropped to 0.25 per cent, in the last year to 0.17 per cent and in the first ten months of 1946 to 0. We have now prepared 660 patients for surgery with one of these three agents with but one

death, and that a coronary thrombosis which occurred on the second day after the patient had made an excellent operative recovery from the subtotal thyroidectomy.

A very graphic example of what these patients can do is illustrated by a patient whom I have often described. She was a lady of 77 with 30 pounds weight loss. She had auricular fibrillation, heart failure, and was a diabetic. She had a metabolism of +44. She would have been a very bad risk prior to the time these drugs were available, but when she was put on thiouracil, the metabolism dropped to +1, the heart became regular, her compensation was restored, the diabetes was easier to treat, she gained 8 pounds in weight, had a subtotal thyroidectomy, and at no time did she have a pulse rate over 80 postoperatively or a temperature reaction. If you will compare this patient with what the problems would have been prior to the employment of these agents, it will graphically illustrate how we have been aided in dealing with the patients who have serious complications, such as heart failure, diabetes, tuberculosis, pregnancy, or any of the other complications.

We have also learned that one cannot depend upon the time period for complications. We have seen patients go along with no difficulties whatever and then as late as the ninth month, develop an agranulocytosis. Note that these complications are: depression in the white blood cells and differential counts, fever, skin eruptions, edema of the skin, salivary gland reactions, and there has recently been reported a patient who developed a pancreatitis that required exploration because it is known that the administration of these drugs likewise promotes hyperplasia of the pancreas.

It has been stated that the present employment of thiouracil over the country has produced a mortality higher than occurs with good thyroid surgery. We believe one of the disadvantages of the prolonged administration of these drugs is that you cannot predict at what time an agranulocytosis may occur; the patients must always be in danger of this possibility and must always be close to adequate laboratories

where they can have white and differential counts.

We have employed these agents in 21 cases to determine whether or not they would promote permanent remissions. In 8 young individuals with very low metabolisms who had had mild hyperthyroidism and had had it but a short time, permanent remissions have occurred, but in all of the others, reappearance of the hyperthyroidism has occurred as soon as the administration of these drugs was stopped.

OUR OWN medical department believes that the percentage of recurrences on omitting these drugs is so high, that we do not feel interested in the use of this drug as an agent to be used as a substitute for surgery.

I do not mean particularly to be prejudiced in favor of surgery nor do I defend it against thiouracil, but wish only to compare it. Up to ten years ago we had a recurrence rate following subtotal thyroidectomy of 7 per cent, which was by far too high. We now have a rate which is under 1 per cent and the mortality rate, as has already been stated, is 1 death in the last 660 cases. We have practically abolished tetany and recurrent laryngeal paralysis. When one therefore considers our recurrence rate, the danger of the use of thiouracil in place of surgery, the risk of agranulocytosis, the necessity for frequent white counts, the fact that agranulocytosis can occur at any period of the administration, we believe that from our point of view, surgery continues to be the safest, most positive, and most satisfactory method of treatment.

We believe that it will be possible to give up thiouracil and thiobarbital now because propyl thiouracil is so much safer. In view of an incidence of 9 per cent complications with thiouracil, 28 per cent with thiobarbital, and only 2 per cent with propyl thiouracil, we believe the former two should be abandoned.

We would like again to stress that the combination of iodine throughout the administration of thiouracil is more effective in prompt action than the use of thiouracil alone.

We would like to call attention to the fact that when patients are sensitive to propyl thi-

ouracil one may occasionally change to thiouracil and carry them through without reactions.

When complications such as agranulocytosis or neutropenia occur, there is but one drug that can be depended upon, and that is penicillin. Pyridoxine (B_6) is of no value; liver extract is of no value. What happens when you get an agranulocytosis is that the bone marrow is unable to produce the protective elements in the blood to deal with it; therefore, you must use some agent to deal with the infection while, by omission of the thiourea drug, the bone marrow recovers its capacity. It is obvious that one must be particularly on the lookout for patients who have low white counts, below 4,500, and differential counts below 45 per cent neutrophils, and particularly those who develop sore throat.

I wish to stress again that pancreatitis has been reported, due to hyperplasia of the pancreatic cells, and during the administration of these agents one must watch for pain in the abdomen.

One other thing I would urge, although I think it is probably not very practical, is that, if possible, in any hospital where this treatment is being used, it should be put in the hands of one or two men. That means they get the experience with it so that they can protect the patients.

ANOTHER point to bear in mind is that the fever reactions which occur with these drugs are associated with joint pains, back pains, nausea, vomiting, and that they are true sensitization reactions.

Also of interest are two other thyroid conditions which we have encountered during the last year or two. They may occur in your experience and you should, therefore, be conscious of them. One is the thiocyanate goiter. Thiocyanates are known to be goitrogenic in character and are the kind of goiter that will occur in the experience of some of you before the year is over. Unless you know about it, you can be greatly confused and can get into difficulty with it. Potassium thiocyanate is being used, as you know, for hypertension. It is a goitrogenic

agent; it will produce enlargement of the thyroid gland and will ultimately produce myxedema. It is like the thiourea group. We have had two of these types of thyroid enlargement incited by potassium thiocyanate. They produced so much enlargement well down to the mediastinum and compression of the trachea that until we found out what it really was, the patient was threatened with a tracheotomy.

Because it enlarges the thyroid and produces myxedema, the thiocyanate goiter can also definitely interfere with breathing. You must be on the lookout, therefore, for patients who have been under blood pressure treatment with potassium thiocyanate as to the possibility of a thiocyanate goiter and its producing interference with breathing.

You need only stop the treatment or give them thyroid extract; the gland will promptly go down and they will regain their ability to breathe all right.

The other type of thyroid disease has also occurred in the last two years and is the hyperthyroidism with a normal metabolism. How can it happen? In occasional cases the normal metabolism may be a minus one. We have had a patient who had a -34 who had no myxedema at all. She did not have a high blood cholesterol, but when her metabolism was at $+4$ or $+5$ she had hyperthyroidism. Her blood cholesterol was low, she had all of the clinical symptoms, and following subtotal thyroidectomy, with a return of the metabolism to -34 , she was perfectly normal.

We have also had another case with a normal metabolic rate but with all the clinical signs of hyperthyroidism and with a low blood cholesterol, tachycardia, tremor, exophthalmos. When she had a subtotal thyroidectomy she too had convincing drops in metabolism to minus degrees, but this was her normal metabolism and there was marked clinical improvement.

Do not be misled at the inclusion of occasional patients who have very definite clinical hyperthyroidism because they can have a normal metabolism which for them is an elevated metabolism if their normal metabolism is of a low minus character.

Treatment of Pernicious Anemia

RUSSELL L. HADEN

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THIS discussion will be limited to the treatment of pernicious anemia, a disease which is very poorly handled, although there is a specific for it. Five case histories will be set forth, and I shall make some comment about the diagnosis of the disease, tell you how I think it should be treated, and show you what results our patients have had with such treatment.

The first patient has been under my care since September 30, 1931. A diagnosis of pernicious anemia had been made in 1928, three years before I saw her. She could not have been treated very well, because when I saw her she had only a little more than a million red cells and 32 per cent hemoglobin. From 1928 to 1931, although the diagnosis of pernicious anemia was evident, she had had a hectic time with many ups and downs and had undergone thyroidectomy for tachycardia. The thyroidectomy was of no real value to her, since the symptoms for which the operation was done were caused by pernicious anemia.

She had had the usual signs of weakness and other symptoms of anemia, and during that period developed a cord lesion. When I first saw her she could hardly walk. She had such a marked involvement of the lateral columns of the spinal cord that she could only shuffle along; she could hardly lift her feet off the floor and was unable to walk upstairs at all. I emphasize the neurologic status because this

case shows one greater danger of incomplete treatment and also shows what marked improvement one can get in the neurologic lesions of pernicious anemia with proper treatment.

She had a large spleen which is very unusual in pernicious anemia. In our series of more than 600 patients not more than 5 per cent have had an enlarged spleen. Splenomegaly is always against the diagnosis of pernicious anemia. She did have a very smooth, glossy tongue. The first thing that I do when examining a patient with anemia is to look at the tongue. I once thought that when a doctor looked at the tongue he didn't know much medicine. I now think that he knows a lot of medicine when he does.

In addition to the curious shuffling gait she necessarily had hyperactive tendon reflexes in the knees and ankles. She had a bilateral positive Babinski reaction and marked ankle clonus. The vibratory sense was entirely lost up to her hips.

Treatment was started by the method set forth below. Her blood quickly returned to normal and has remained normal for the last fifteen years. She comes in every little while for an examination and blood count. Her blood count has always been normal.

Before treatment, what did her blood show? There was an anemia with large red cells. The most characteristic thing about the blood in pernicious anemia is the large red cells. There is always a macrocytic anemia in an active untreated pernicious anemia. Not infrequently patients are treated for pernicious anemia when

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make the diagnosis of pernicious anemia because the patients have usually been given liver extract without an adequate study. The first thing to try is a test meal if the patient has been treated. If acid is present he does not have pernicious anemia. If he has no free hydrochloric acid, pernicious anemia may or may not be present.

These three patients had well-marked pernicious anemia. I treated the first with liver extract by the method we have been using for many years. The second had 10 mg. of folic acid by hypodermic injection; the third had 20 mg. given by the same schedule instead of liver extract. Interestingly enough, these three patients all got exactly the same final result. With folic acid the reticulocyte count does not rise to the level calculated from the use of liver extract, but so far as I can see, the results are exactly the same.

SHOULD we use folic acid? I do not know. It is new. I, for one, shall stick to liver extract until we know more about folic acid and can determine exactly what role it will play. All of us are hoping that folic acid may give a better result; that it may have a greater effect on the neurologic manifestations of pernicious anemia than liver extract has produced. I doubt it because I think the trouble with the management of the neurologic manifestations of pernicious anemia has been that the treatment has not been carried out properly.

It takes about three months for the blood to return to normal. After only two and a half months one patient's count was 4,350,000 and her hemoglobin 81 per cent. She still has a volume index of 1.07. You may say that this doesn't amount to much, but it certainly does. It means that she still is not well hematologically.

How should liver therapy be given? Liver extract parenterally is the treatment of choice. We are all besieged by the detail men with extracts of all sorts of potency. I have in my files the advertisements of all the major pharmaceutical houses, each with a number of ex-

tracts. The potency must always be kept in mind.

A unit should be the amount of specific principle needed to supply one person for one day. We have always used an extract containing 15 units per cc., which is the ordinary concentrated preparation. Another manufacturer will have one with 10 units, others with 3 and 5 unit extracts. I don't see any sense in that whatsoever. I see no point in using an extract containing less than 15 units per cc. The material is stored in the body and not rapidly excreted. It is important to select an extract that you know is good, that you can depend upon, and then stick to it.

It is a good investment for the patient to spend the first two weeks of treatment in the hospital. Pernicious anemia is a very serious disease. Before 1926 all patients who had it died. A stay in the hospital emphasizes to the patient the seriousness of the disease. During this two-week period an intramuscular or subcutaneous injection of 15 units of a known potent liver extract is given daily. At the end of this time we start similar injections of the same amount twice weekly for three months. The next three months 15 units are given weekly; the next six months 15 units, twice a month. This covers treatment for the first year. One injection of 15 units is given monthly for the rest of the patient's life. With intercurrent disease, more frequent injections are required.

All of our patients understand before we discharge them that we have not cured their disease; we have simply returned the blood to normal. We emphasize that they have to take specific treatment for the rest of their lives.

The length of time that a patient can go without recurrence of symptoms in the absence of treatment of pernicious anemia is extremely variable. As a rule, the anemia and other symptoms recur in a few months at most. Recently we had a patient return who had had no treatment for five years. After her blood returned to normal, she had discontinued injections. She again had marked anemia, but had gotten along quite well for five years. This is the unusual. To discontinue treatment is dangerous.

What you do with this disease is to supply a deficiency which the patient can never supply himself since there is an unalterable defect in the stomach mucosa. You should use a potent liver extract and, at the beginning of treatment, give it intensively. The treatment must be given for the rest of the patient's life.

This method of treatment, while intensive at the start, requires fewer injections in the long run than the usual method. It is not necessary to give injections frequently after the preliminary period of intensive therapy. I often see patients who have been given injections of liver extract twice weekly. This is not necessary.

I come back to the tongue again because I cannot mention it too often. If a person has a tongue with long papillae and a little coating, it is perfectly normal. There is not one such person in a million with active pernicious anemia. On checking patients, one can often tell their need for liver extract simply by looking at the tongue. A clinician should never overlook the inspection of the tongue.

The blood should be studied regularly. If the patient follows the treatment suggested, the blood will be perfectly normal all the time. I tell our patients that every three to six months they should have a complete blood study because we can quickly tell in the laboratory whether the treatment is sufficient or not.

All pernicious anemias during the active stage are macrocytic. That means the cells are large. A macrocytosis develops long before there is an increase in the color index, which is often emphasized but is dependent on the in-

crease in cell size. To determine the red-cell volume a hematocrit reading is made after centrifuging a fixed amount of blood. The mean cell size is calculated from this simple data. The size of the normal cell is 90 cubic microns and the normal volume index is 1.00. If a person develops pernicious anemia, the red cells get larger.

If liver extract is given to a patient who has a macrocytosis that is caused by the lack of the specific principle supplied by liver, the red-cell size returns to normal.

Iron has exactly the opposite action to that of liver extract. Iron makes the cell larger, not smaller, by filling the cell with hemoglobin. A normal cell with an iron deficiency becomes smaller. The mean volume here is 66 cubic microns, so the volume index is 0.73. With iron, the cell becomes larger and returns to normal.

Is hydrochloric acid given? No. Nobody wants to take hydrochloric acid unless he has to. So far as I can see, it doesn't help a bit in pernicious anemia unless it is indicated for some symptom such as diarrhea.

Should iron be used? No. Iron and liver should rarely be given at the same time except to some person who has both an idiopathic iron deficiency and an idiopathic pernicious anemia.

In conclusion, I wish to emphasize again the marvelous results one gets in the treatment of pernicious anemia by proper diagnosis and treatment. Liver extract is the specific method of treatment which should be used for the present. The place of folic acid in the treatment of this disease is still undetermined.

in symptoms of obstruction. Bladder stones may become impacted in the vesical orifice. A large stone may interfere with urination because of its proximity to the bladder-neck and hence produce symptoms of obstruction. Dumbbell-shaped stones with one part in the bladder and the other part in the prostatic urethra produce very severe symptoms of obstruction.

Certain bladder tumors produce obstruction and difficulty in urination, such as pedunculated papillomata fibromata, and muscular tumors. In an occasional case a long pedunculated polyp may produce symptoms of obstruction. In these cases it is possible to obtain a history of interruption of the urinary stream.

Carcinoma of the bladder may involve the internal ureteral orifice and produce symptoms of urinary obstruction. A tumor with its origin in the trigone or a cyst of the trigone may produce obstruction. Some of these pedunculated tumors may have their origin in the dome of the bladder, and a large tumor impedes or obstructs the bladder-neck so that the patient has great difficulty in urination and in some instances may even develop complete retention.

CYSTS of the trigone are rare and are mentioned only to call attention to the fact such a lesion does occur and that in an occasional case it may produce symptoms of bladder-neck obstruction.

Hypertrophy of the interureteral ligament may produce obstruction. This is generally due to obstruction at the neck by changes in the prostate. Unless this condition is recognized, the patient may continue to have symptoms after the prostatectomy.

Although lesions of the ureter producing obstruction to urination are rare, they do occur, especially in children. They occur with sufficient frequency to bear them in mind. I refer, of course, to so-called cystic dilatation of the vesical end of the ureter, sometimes called ureterocele. I have seen cases in children in which the ureterocele completely filled the bladder, resulting in complete retention. As a result of the tenesmus, the ureterocele may

protrude from the external urethral orifice in girls.

Lesions of the central nervous system may produce obstruction to urination. The possibility of their occurrence must always be considered. Errors in diagnosis may easily occur unless careful search is made. Patients with *tabes dorsalis* have had bladder operations. Some of the patients belonging to this group, because of their bladder symptoms, have had long courses of local treatment with no relief of their symptoms. The various types of lesions of the central nervous system are too numerous to mention. I have already called attention to the fact that *tabes dorsalis* may be overlooked. The patient with pernicious anemia may have degeneration in the spinal cord with resulting urinary symptoms.

Spina bifida, tumors of the spinal cord, extrapyramidal tract lesions, multiple sclerosis, myelitis, and spinal cord injuries may also be responsible for the symptoms of urinary distress. Because of the present-day wave of enthusiasm for disc operations, may I point out that I have seen three patients who developed complete retention following this operation. The management of this type of patient presents many interesting problems, particularly the so-called spinal cord bladder, the result of war injury.

I would like to point out that the patient with *tabes* may also have a bilateral enlargement of the prostate. Formerly patients with this combination were advised not to have a prostatectomy because the prostatectomy would be followed by incontinence. This was unfortunate. I have performed suprapubic prostatectomy on 6 to 8 tabetics, and they did not develop incontinence. At the present time a patient with this combination can be relieved by transurethral resection.

Lesions of the gynecological tract producing urinary symptoms, especially those of obstruction, are relatively common. As a matter of fact, it is because of the urinary difficulty that the patient first consults the urologist. It therefore becomes increasingly important that women having symptoms of urinary obstruc-

tion undergo a careful urological examination as well as a thorough gynecological examination. In my experience it is not at all infrequent to have a patient consult me for symptoms of bladder-neck obstruction when the cause of the symptoms may be rather a large cystocele and rectocele.

Patients with large fibroids impinging on the bladder often have great difficulty in urinating. Certain types of small fibroids, depending upon their direction of growth, may likewise cause bladder-neck obstruction. Carcinoma of the uterus and large ovarian cysts may also be responsible for symptoms of bladder-neck obstruction.

Lesions of the rectum producing this picture are uncommon. However, large benign and malignant lesions of the rectum and occasionally a large diverticulitis of the bowel bring the patient to the doctor because of symptoms of obstruction.

TREATMENT

TREATMENT of bladderneck obstruction consists primarily of diagnosis. It must concern itself with determining the cause of the symptoms and the location of the underlying pathology. It is perfectly obvious that the institution of treatment under any other premise gets one nowhere. It is a waste of both doctor's and patient's time to institute local treatment to the bladder when the primary pathology is due to a marked cystocele or a large fibroid. It is equally fallacious to treat with bladder instillations the patient who has bladder symptoms due to spinal cord changes arising from pernicious anemia. On the other hand, a patient may have two lesions producing symptoms of bladder-neck obstruction, namely *tabes dorsalis* and prostatic enlargement. This patient should have a transurethral resection just as though he had no *tabes*. The patient with *tabes* can now be relieved of his difficulty, frequency, residual urine, and infection by means of a transurethral resection.

The patient with benign prostatic obstruction is treated by means of transurethral resection.

The number of patients who today are subjected to suprapubic or perineal prostatectomy is very small. More and more patients are treated by transurethral resection because the mortality rate is lower, the stay in the hospital is shorter, and complications occur less frequently with resection than with suprapubic prostatectomy. In an occasional case, when the prostate is very large, it may be necessary to perform a second resection. When one cannot introduce the resectoscope, it may be necessary to proceed with a suprapubic prostatectomy. One of the patients I discussed previously had a resection with temporary relief. Because the symptoms returned and because of the size of the prostate, a suprapubic prostatectomy was deemed advisable.

A patient with stricture of the urethra and prostatic enlargement should have the benefit of urethral dilatation before proceeding with the resection. In some instances dilatation of the stricture is all that is needed.

Patients with carcinoma can be treated with resection to relieve the obstruction. The advisability of this depends on the severity of the symptoms, the amount of residual urine, and the presence or absence of infection. After resection these patients should be given stilbestrol by mouth. If the symptoms recur, they may require a second resection. Castration for carcinoma of the prostate has lost its popularity and is on the wane.

Radical operation—that is, complete prostatectomy, seminal vesiculectomy, and removal of the bladder-neck—has its advocates. The drawback to this treatment is that many of these patients come in late in the course of the disease, when the carcinoma has already spread beyond the confines of the capsule of the prostate.

Prostatic calculi may be treated by perineal prostatotomy, or, if they are large or deep-seated, by transurethral resection. In most cases where operation was indicated I performed transurethral resections.

Abscess of the prostate should be treated by perineal prostatotomy. Prostatic cysts can be destroyed with the high-frequency current.

Uterine Fibroids

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I AM TAKING the subject of fibroids because fibroids are so exceedingly common. Also, they may appeal to many of you as one of the major sources of income to the profession, unjustifiably in many cases, and that is what I want to stress.

Fibroids are perhaps the commonest of major tumors. Graves makes the statement that 40 per cent of all women will have fibroids during their lifetime and that practically all single women of middle age may have them. Cullen, on the other hand, in investigating the records at Hopkins Hospital, said that of all the women who had come to autopsy over 20 years of age, 20 per cent showed fibroids. This figure is rather unfair because we don't usually see fibroids in women before the age of 30; so many of those women who were autopsied between 20 and 30 who showed no fibroids probably would have developed them with age.

Fibroids are more common in the nulliparous than in the parous woman. It may be that the fibroid has caused the sterility. On the other hand, some wag has said that it is simply frustration on the part of the womb, that the uterus says to itself, "Hang it all, if I can't make a baby I'll do the next best thing, I'll grow a tumor."

The colored race is particularly susceptible to fibroids, and in our clinic we assume that

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any middle-aged negress who comes in, whatever else she may have in the way of pus-tubes or tubal pregnancy, at least will probably have a fibroid.

Fibroids always begin as small nodules, single or multiple, in the wall of the uterus. They are composed of the same elements as the uterus, namely, muscle and fibrous tissue, and are definitely demarcated from the adjacent myometrium. The fibroid is thus analogous to a lipoma in adipose tissue. Why lipomas become discrete and more or less encapsulated we do not know. We do not know the real cause of the fibroid; nothing has ever been adduced to explain it.

Fibroid tumors may vary from microscopic to very large in size. Cullen reported one of 89 pounds, which was the largest reported up to that date. They are practically always in the corpus of the uterus, very rarely in the cervix. If they are in the cervix, they are usually small but are apt to prove more complicated at operation.

These intramural tumors do not remain in the wall of the uterus. They tend to migrate. One reason may be that they grow toward an area of less resistance, either toward the peritoneal surface or into the cavity of the uterus. I think a very important factor in migration is the rhythmic contractions of the uterus, which tend to squeeze the nodules either internally or externally. We know that the uterus is rhythmically contracting all the time. These contractions become particularly increased in



William H. Weir

dysmenorrhea. Labor pains are simply exaggerations of them.

These contractions tend to squeeze the nodule either internally or externally, producing either subperitoneal or submucous fibroids. By far the least troublesome is the subperitoneal nodule, because it will practically never cause bleeding. When the tumor approaches the cavity of the uterus it usually leads to a hypertrophy of the mucosa, and bleeding comes from the mucosa, not from the tumor. It may come from the tumor in the case of necrosis of a submucous pedunculated fibroid, but is nearly always endometrial.

As the tumor is expressed from the wall of the womb into the peritoneal cavity it forms a pedicle. This pedicle may become narrower from the contractions so that the circulation is apt to be more or less cut off, and there may be a necrosis of the subperitoneal nodule. There is nearly always what is really a necrosis, hyaline degeneration, in a fibroid of any size. The whole nodule may be visibly degenerated, or it may be microscopic. When the circulation through the pedicle becomes impaired, there may be adhesions formed to the omentum. New vessels will grow from the omentum into

the nodule and ultimately nourish it. The pedicle may become completely severed, resulting in a "parasitic" fibroid, a fibroid that began in the wall of the womb and ended by having no anatomic connection with it at all.

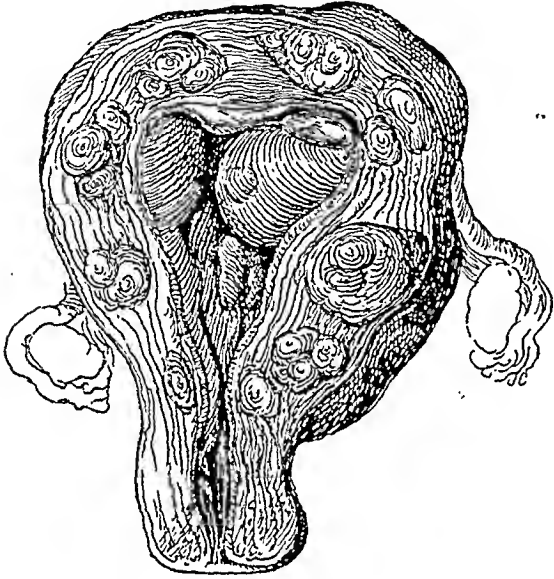
Similarly, a tumor in the cavity of the womb becomes pedunculated, really forming a foreign body inside the uterus; the contractions are increased and it is expelled as any foreign body might be. The pedicle elongates, becoming longer and longer; the tumor dilates the cervix, enters the vagina, which may be greatly distended by the tumor. Finally the pedicle may part and the tumor be expelled, resulting in what one might call a spontaneous cure of a fibroid.

AN INTRALIGAMENTARY fibroid is one that has grown outward from the uterus and happened to develop between the walls of the broad ligament. It is in no way different from any other except in the operative difficulties which it may offer. Like a parovarian cyst, it may lead to tremendous elongation of the tube, but the main danger is from distorting the relation of the ureters, which may be damaged in operation.

There is one other type of tumor closely allied to the ordinary fibroid, and that is the adenomyoma, which differs in the fact that scattered through it are areas of endometrium. It is more of an endometriosis than a true fibroid. It offers difficulties in myomectomy because it is not well defined. Usually fibroid nodules are sharply defined, so that they can be easily shelled out, but the adenomyoma shows no definite capsule and is much more difficult to handle.

What happens to these fibroids? As a rule they grow slowly. Sometimes they grow rapidly, which leads to the fear that they may be malignant. They may be subject to rapid increase of size as a result of sudden edema, particularly generalized edema, which may subside later. Not infrequently in the case of medium-sized fibroids, one may find the fibroid slightly increased in size before the period, and it may regress afterward.

These tumors may undergo slow growth or remain stationary until the menopause, when they behave exactly as the rest of the uterus does—they atrophy. It doesn't make any difference whether the menopause comes on naturally or is induced by radiation or surgery. In the early days of surgery, hysterectomy was regarded as a very dangerous operation but



Multiple Fibroids

ovariotomy was much simpler, so they simply removed the ovaries.

These tumors tend to degenerate. They have a very poor blood supply. The common degeneration is the so-called hyaline degeneration, which is really a necrosis. The whole tumor loses its vitality, but fortunately the presence of the dead tissue rarely does any harm. As a consequence of the degeneration there may be more or less calcification, so that sometimes a large fibroid may be turned into a stony mass which cannot be cut with a knife but may be divided with a saw much as you would soft marble.

One may find also myxomatous degeneration. This soft dead tissue may liquefy and form large cysts in the substance of the tumor.

There is a particular degeneration for which one must be on the lookout, the so-called acute red degeneration, which is particularly prone

to occur in pregnancy. It is an acute process. One patient I saw not long ago had a large fibroid the size of a coconut. She suddenly developed an acute abdomen with rigid abdominal walls, severe pain, high fever, leukocytosis—all the things which may occur with an acute infection. I suspected red degeneration. We waited a few days until the acuteness of the process subsided and then operated.

THE DEGENERATION we fear is of course, sarcoma. Textbooks very often stress this a great deal and I think very unwisely, because sarcomatous degeneration rarely occurs. The microscopic picture in many of these fibroids is misleading, and one cannot depend upon every pathologist's report. A rapidly growing, cellular fibroid may give exactly the picture of a sarcoma. More important is the clinical record of the case, because if you have a sarcoma of the uterus you are rarely going to get rid of it by operation. Very early there will be multiple adenomyoma, which differs in the fact that metastases, as the clinical records usually reveal.

I looked over our records at the University Hospitals and found that in the last twenty years there were 328 cases of malignancy involving the corpus of the uterus. The vast majority of those were adenocarcinoma originating in the endometrium. Of these 328 cases, there were only 7 that showed any sarcomatous change. Five of these 7 happened to have fibroids, but in no one of those 5 was there any evidence that the sarcoma had started in the fibroid.

Opinions vary as to whether fibroids predispose to the development of adenocarcinoma, which of course must originate within the endometrium, since there are no epithelial elements in the fibroid. Of course, if 40 per cent of women have fibroids, you are going to find them in a great many adenocarcinoma cases, but that is not proof that the fibroid had anything whatsoever to do with the development of the carcinoma.

What symptoms do patients with fibroids have? Often they have none whatever. An instance is the case of a young woman who went

to join a gymnasium class, and the doctor looked her over lest she might have a heart lesion. He referred her to me because she had a tumor. The tumor extended up below the costal margin. It happened to be flat, so the slightly enlarged abdomen was perfectly smooth, and she didn't even know that she had a lump there. I went over her with a fine-toothed comb and could find no menstrual disturbance, no pain, no disability whatever.

Another patient said, "Doctor, there is nothing wrong with me except that my clothes won't hang straight." When she stood up, she looked as if she were going to have triplets the next minute, which was very embarrassing for an unmarried school teacher. In that case, except for a huge fibroid, the only abnormality I could find on examination was slight edema of the ankles.

BLEEDING is the common and outstanding symptom of fibroids. It comes from the endometrium, which is usually hypertrophied. It may be far more dangerous and profuse in the case of a submucous tumor, and if such a tumor becomes ulcerated or degenerated, the bleeding may come from the tumor itself. Nearly always, however, the hemorrhage is endometrial.

The bleeding recurs with every period; the woman may lose more blood at each menstruation than she can quite make up during the interval; there is a gradual increase in the anemia at every period, but perhaps not so rapidly as to attract her attention.

In addition to bleeding she may have pressure symptoms, which may be simply a dragging-down due to the weight of the tumor, such as occurs with an ordinary uterus if the perineal supports are inadequate. Undue strain on the supporting ligaments of the uterus may lead to reflex nervous symptoms or the tumor may give rise to pressure, causing pain down the legs, and backache. Urinary symptoms may develop from crowding the bladder, but are often due to the fact that these large tumors nearly always cause some degree of hydroneph-

rosis by pressure on the ureter, and the bladder symptoms are reflex from that.

Large tumors may cause edema of the ankles and varicosities, just as will the pregnant womb. They may produce a leukorrhea because the endometrium is hypertrophied and there is more secretion, usually a thin, watery fluid, but in the case of a necrotic submucous fibroid there is a foul, ill-smelling discharge which may closely resemble that of carcinoma.

Sometimes there may be really acute pain due to red degeneration or to torsion of a pedunculated tumor or from tension on bowel adhesions or other adhesions internally. At times an infection of a degenerated fibroid may occur when the tumor is adherent to the bowel, although in a necrotic tumor, otherwise aseptic, the germs may reach it through the blood stream.

The diagnosis of fibroids is usually easy in most cases, though sometimes it may be exceedingly difficult. The thing about which we have to be very careful is pregnancy, especially where the tumor causes a symmetrical enlargement. Frequently a fibroid and also pregnancy are encountered. If the tumor is large and very nodular, anybody can feel it, although the same nodular feeling may be presented by a multilocular ovarian cystoma.

In cases that have been referred to me by other doctors I have found that a very common error is to mistake a retroverted uterus lying back in the cul-de-sac and perhaps somewhat hypertrophied, for a fibroid. I have had many of those come to me diagnosed as fibroids when they were simply retroversions. Any inflammatory mass in the pelvis may resemble a fibroid and cause a mistake in diagnosis. No one can feel the very small fibroids, and even when they get larger, the diagnosis may be very difficult.

In one very interesting case of bleeding from the howel, I did an exploratory, and there was a fibroid about an inch and a half in diameter so densely adherent to the right cornu of the uterus that it had to be separated by sharp dissection. It was not a uterine fibroid. It was a

fibroid of the terminal ileum, which accounted for the bowel bleeding and which, in some inexplicable way, had become adherent to the uterus.

Occasionally you may examine a slightly symmetrically enlarged uterus and fail to diagnose a fibroid, and at a later visit there, in the cervix or actually lying in the vagina, is a submucous fibroid which has delivered itself and is now perfectly obvious.

The treatment is the important thing. In most of these cases a "policy of masterly inactivity" is all that is necessary. The small or medium-sized tumors may not be causing symptoms, and they may have been discovered in a routine examination, not infrequently because the patient comes in for sterility, and the examination reveals the tumor.

A favorite question of mine in examining students is what they would advise if a young woman 30 years old comes in wanting a premarital examination and some contraceptive advice and they find a fibroid tumor of the uterus a couple of inches in diameter but causing no symptoms. Of course many of them want to operate. The answer I want is to do nothing but to advise that young woman not to use any contraceptive measures and to try to become pregnant just as quickly as she can. In a few years the tumor may have grown or other complications may have developed so that she cannot then become pregnant.

Then comes the palliative treatment. How are you going to deal with the bleeding? The first thing you use, provided the tumor is of moderate size and is not causing too much trouble otherwise, is drugs. For this purpose, ergot or ergotrates are often used. I depend largely upon fluid extract of Hydrastis in 15 drop doses, or stypticin, which is a closely allied drug. In recent years, testosterone has been found very efficient in these uterine hemorrhages, giving about 25 mg. hypodermically every day or so, but not using more than about 300 mg. in any one month, for fear of producing masculinizing symptoms.

IF THE medicine does not control the bleeding, the next step naturally would be a curettage. In a great many cases we want to do the curettage for other reasons, too. These tumors develop in the cancerous age and the woman may have a fibroid, but she may also have a cancer, and we want to be sure, if we are going to treat the case palliatively, that there is no cancer.

The curettage is often difficult because the tumor may have enlarged the cavity and it may be so irregular from projecting fibroids that you cannot adequately curette the whole surface.

I have curetted a case and had to take the uterus out soon afterward, finding a big polyp that had evidently been pushed aside by my curette and not removed. I would strongly advise using a ring forceps. Put the ring forceps up into the cavity, open and then close it, and you may grab a pedunculated fibroid or mucous polyp which you can twist out with perfect safety.

You must correct the anemia, either by iron or liver, et cetera, and not infrequently you may even have to give a transfusion.

We radiated one patient who should have been operated upon but who refused operation, and while we were waiting for the effect of the radiation she had another period and almost bled to death, needing repeated transfusions until the radiation became effective.

For the dragging and pain you can do certain things. I have found great relief comes in some cases from simply putting in a pessary, which will take the weight off the ligaments. If there is a retroversion and you can correct that, it may help a good deal. Particularly in the case of tumors that are incarcerated in the pelvis, you may be able to work them up above the brim of the pelvis where there is more room and give the patient considerable relief.

The palliative treatment is particularly indicated in younger women who have not had but want children and in whom you do not wish to destroy the child-bearing function. There are other women who flatly refuse to

have anything done, either radiation or operation, and you have to do the best you can under those circumstances.

Next would be conservative surgery. You want to preserve the child-bearing function. For this purpose we do a myomectomy. I do not like doing myomectomies because if you do it to promote pregnancy, the patient, having had an abdominal operation, fully expects to become pregnant. You cannot guarantee it, because some other factor may have been preventing the pregnancy. However, if the fibroid is bleeding and is liable to interfere with pregnancy, we do a myomectomy. I always warn them very carefully, "We may take out every last fibroid we may find and in a year or two you may have a lot of others."

RECENTLY I had two patients in one room, side by side, with large bleeding fibroids requiring hysterectomy. It so happened that exactly 13 years ago I had operated on both of them, doing a conservative myomectomy. In the interval one had had a baby. You must always warn your patient that if you do a myomectomy they may develop other fibroids, which may have been present at the time of operation but were too small to be recognized.

If myomectomy is not feasible, you have to do something more radical. The simplest radical procedure—and I mean radical, because it destroys the child-bearing function—is radiation, which may be done by inserting radium in the cavity of the womb. This is often awkward because the cavity may be large and irregular. Practically, I find that radiation by deep x-ray therapy is just as efficient and has many advantages. It is very simple, much less expensive, absolutely safe, or as nearly safe as can be, and does not hospitalize the patient; the patient need not give up her job, but can go right on with her work. The treatment is very effective.

Radiation is not usually advised in large tumors. They should be removed because of the danger of hydronephrosis from pressure on the ureter. Any large tumor ought to come out, but a tumor not over the size of a three-and-a-

half-month pregnancy can be very adequately radiated. Radiation does not remove the tumor, it is still there, but it becomes much smaller and practically never causes any subsequent trouble.

I do not see any reason why inducing the menopause is going to do the woman any harm. She has to go through it anyway; she cannot avoid it. I do not think a menopause induced by radiation is in any way worse than the natural one.

Next is radical operation, and I believe in a *radical* operation. I take out the whole womb, cervix and all. The cervix is a great troublemaker. You cannot tell anything about the cervix from the look of it; it may be chronically inflamed and yet look perfectly normal. I have no sympathy whatsoever with the man who does a supravaginal hysterectomy and leaves a small amount of endometrium so that the woman will continue menstruating for her own satisfaction. I never yet saw a woman who, if you explained things to her satisfactorily, was not tickled to death to get rid of this messy, unnecessary function of bleeding every month. You have to explain why the menses are not necessary to her health.

In dealing with fibroid tumors therefore, the majority of small- or moderate-sized tumors which are causing no symptoms need no particular attention other than keeping them under supervision until after the menopause. If symptoms such as simple bleeding occur, medication may be all that is necessary or a curetting may also be indicated. In women desiring children, conservative treatment should be used if possible and this may necessitate a myomectomy. If the symptoms cannot be controlled by such measures and the tumor is not too large, radiation may be required. Many small- or moderate-sized tumors that might easily be radiated had better be removed by operation if there are other reasons for an operation, such as a relaxed vaginal outlet or other birth traumata. The large fibroids should always be removed on account of the danger of hydronephrosis.

ence or absence of the secretory factor may have some bearing on the low incidence of erythroblastosis due to AB incompatibility of mother and child.

In 1940 Landsteiner and Weiner discovered the Rh factor, so named because the antibody was first obtained by injecting blood from the *macacus rhesus* monkey into rabbits. When this antibody was tested against human blood, the cells of 85 per cent of Caucasian individuals were agglutinated. In other words, 85 per cent of human beings had the Rh antibody in the blood, and 15 per cent did not. The Rh factor is dominant and never appears in a child's blood unless present in the blood of at least one parent. The Rh factor is like the M and N factors and unlike the A and B factors in that no natural Rh antibodies occur in sera. Unlike M and N factors, however, the Rh factor is highly antigenic to human beings, although there are gradations within this antigenicity.

The Rh blood group is of the utmost importance with respect to transfusion reactions. The first transfusion of an Rh-negative individual with Rh-positive blood would produce no reaction since the patient had not as yet been immunized. Repeated transfusions would most certainly produce untoward reactions, provided enough time had elapsed for development of anti-Rh antibodies. Therefore no Rh-negative female should ever receive Rh-positive blood.

At present, determination of Rh positiveness or negativeness will solve most intragroup transfusion problems. However, two other Rh antisera have been prepared, called anti-Rh' which gives 70 per cent positive reactions and anti-Rh'' which gives 30 per cent positive reactions. The original anti-Rh antiserum has been designated as anti-Rh₀ serum since it is the most important. Because every person is either Rh₀ positive or negative and because there are other less potent antigens in the Rh series, a double scheme of four types can be set up. The table following, taken from Weiner, now becomes as important as Landsteiner's familiar AB table. An understanding of this table gives us the key to most Rh problems.

Since incompatibility of Rh blood groups be-

tween an Rh-negative mother and an Rh-positive fetus is the cause of the majority of instances of erythroblastosis fetalis, it is necessary to understand their heredity. The Rh₀ factor is transmitted as a simple Mendelian dominant by a pair of allelic genes, Rh (dominant) and rh (recessive). An Rh-negative individual would necessarily be homozygous (rh rh) while an Rh positive individual could be homozygous (Rh Rh) or heterozygous (Rh rh). If both parents are Rh negative, all the children must be Rh negative. If one parent is Rh positive and one Rh negative, either all the children will be Rh positive (when the Rh positive parent is Rh Rh) or half Rh positive and half Rh negative (when the Rh positive parent is Rh rh). When both parents are Rh positive, all the children will be Rh positive unless both parents are heterozygous (Rh rh) in which case three-fourths will be Rh positive and one-fourth Rh negative.

SCHEME OF THE EIGHT RH BLOOD TYPES

Designation of Types	Reaction with Antiserum		
	Rh'	Rh''	Rh ₀
CLINICALLY RH-NEGATIVE INDIVIDUALS (15%)			
rh	—	—	—
Rh'	+	—	—
Rh''	—	+	—
Rh' Rh''	+	+	—
CLINICALLY RH-POSITIVE INDIVIDUALS (85%)			
Rh ₀	—	—	+
Rh ₁ (Rh ₀ ')	+	—	—
Rh ₂ (Rh ₀ '')	—	+	+
Rh ₁ Rh ₂ (Rh ₀ ' Rh ₀ '')	+	+	+

A. S. Weiner. Am. J. Clinical Path. 16:477, 1946.

This scheme is important in discussing with parents who have had one erythroblastotic child, the advisability of future pregnancies. If the father is heterozygous Rh positive, half of his potential children would be Rh negative; thus there is a 50 per cent possibility of obtaining a normal infant. The exact grouping and subgrouping of the parents must be done in a laboratory equipped to carry out such procedures.

Certain incompatibilities of the blood groups

result in a disease in infants known as erythroblastosis fetalis. In order to understand the mechanism of this disease knowledge of the nature of antibody formation in the mother is necessary. For sensitivity to Rh, A, B, or any other factor to develop, the person must first be exposed to the antigen in question. Since erythroblastosis rarely occurs during a first pregnancy, the antigenic cells of the infant presumably enter the maternal circulation during labor and thus may sensitize the mother for any further pregnancy.

Individuals sensitized to agglutinogens such as Rh may form two sets of antibodies, namely agglutinins and/or blocking antibodies or glutinins. According to Weiner the Rh agglutinins like the iso-agglutinins anti-A and anti-B are large molecules and do not pass the placenta readily while the smaller glutinins may pass through. The reaction of the agglutinins on the infant's circulation is clumping while that of the glutinins is usually hemolysis. The clinical manifestations of erythroblastosis fetalis depend upon the type of antibody present in the maternal serum.

Weiner suggests that icterus gravis neonatorum results when maternal Rh agglutinins are milked into the infant's circulation during labor, giving rise to the formation of agglutination thrombi in capillaries and venules of organs where the circulation is slow. The severe jaundice is due to liver damage. Occasionally this syndrome is due to maternal glutinins in the child's blood concomitantly with dehydration of the infant. Other instances may result from AB sensitization.

Rh glutinins, presumably comprised of smaller molecules than Rh agglutinins, more readily traverse the placenta into the fetal circulation during pregnancy and are adsorbed onto the surface of the fetal red blood cells.

The "coated" erythrocytes break down more rapidly than normal erythrocytes in the circulation, giving rise to a gradually progressive anemia terminating eventually with a hydropic stillbirth. The severity of the disease is usually correlated with maternal antibody titer and in milder cases the infant is born alive and can be

saved by proper transfusion therapy with Rh-negative blood. Atypical cases may be caused by the presence of small amounts of the maternal Rh agglutinins resulting in hemolysis, or by AB sensitization.

Snyder believed that some of the instances of feeble-mindedness in institutions may be the result of such Rh sensitivity on the part of the mother, causing brain damage to the infant. On the other hand, others believe that most children who recover from erythroblastosis fetalis will be normal.

A and B antibodies acting on the red cells of infants belonging to a blood group incompatible with that of the mother occasionally bring about a breakdown of their red cells. Because these agglutinins are large and so rarely get into the fetal circulation in great numbers, and because the agglutinogens A and B in the red cells of the infants are incompletely developed, the resulting hemolysis is usually mild. Some cases of physiologic icterus may belong in this category.

Treatment of these allied diseases, which may be grouped under the heading of congenital hemolytic disease, is by transfusion. This is merely replacement of destroyed blood. The accepted amount is 10 cc. of Rh-negative blood per pound of bodyweight when the hemoglobin falls below 80 per cent. Larger transfusions may be necessary when the hemoglobin has dropped far below 80 per cent before treatment is instituted. Care must be taken not to overload the infant, however. Transfusions are not indicated until the hemoglobin falls to 80 per cent. Dehydration should be avoided as it may play a role in the development of icterus gravis neonatorum.

C. A.

1946 PROGRESS IN METHODS OF TREATMENT

ALTHOUGH no one development in medical research in 1946 can be singled out for special recognition or dramatic acclaim, a considerable amount of developmental work was conducted on problems on which fundamental research had been in progress for a long period

of time. Much of this developmental work has culminated in methods of treatment and therapeutic products which have shown experimental or clinical evidence of practical application.

A survey of the medical research reveals a lengthy list of noteworthy advances and we have tried here to review the progress made during 1946 and to indicate the trends for the future.

Details of the structure and synthesis of *folic acid*, the latest member of the vitamin B-complex to be identified as a pure substance, were released in May. In addition to macrocytic anemia with which folic acid deficiency is most commonly associated, other clinical conditions characteristic of chronic deficiencies are leucopenia, hypoplasia of the bone marrow, infections of the intestinal tract, and injury to the mucous membranes.

Streptomycin became available for general civilian use for the first time in 1946 with the greatly increased commercial production. A broad, coordinated investigative project was instituted to study benefits of streptomycin in the treatment of tuberculosis. The value of streptomycin in the treatment of tularemia and certain infections of the urinary tract has also been established by extensive clinical investigations.

Dihydrostreptomycin, derived from streptomycin, was more recently found to have as great activity against germs as streptomycin and to be even more stable.

In November of 1946, announcement was made of the isolation in crystalline penicillin of the active synthetic product and proof of its identity with natural G-penicillin (now called benzylpenicillin). The isolation of *benzylpenicillin* as the triethylammonium salt from the reaction of *d*-penicillamine (*d*- β , β -dimethyl cysteine) and the azlactone (2-benzyl - 4 - methoxymethylene - 5 (4) - oxazolone) proved conclusively that penicillin can be synthesized. The synthesis cannot yet be used as proof of the structure of penicillin as the reaction mechanism is still obscure. Crystalline penicillin having a potency of about 1,500 units per milligram became available in commercial quanti-

ties. During the year, a new preparation of penicillin with a vasoconstrictor was released for the treatment of acute and chronic sinusitis.

Erythrin, a new penicillin-like drug, which is extracted from the red blood cells of rabbits and other animals, is reported to show promise in the treatment of diphtheria and other infectious diseases.

Interest in *tropical diseases* stimulated by the war has resulted in the development of new and improved drugs for their treatment. Superior results have been obtained with Chloroquine (SN 7618) as a suppressive agent and this material has been made available under the name Aralen. Paludrine, introduced by the British, is being subjected to extensive investigation by American workers. More recently, attention has been directed to Pentaquine, an 8-aminoquinoline (SN 3276) which has shown promise as a curative agent in treating relapsing malaria. Clinical investigations are not yet sufficiently comprehensive to establish its superiority over Plasmochin.

Experimental and clinical studies are being conducted on *p*-carbamiodophenylarsenous oxide, the trivalent analog of carbasone, which has shown greater activity as an amebicide than the pentavalent compound. Sodium *p*-melaminylphenylstibonate is reported active against African sleeping sickness; the compound is being tested clinically along with melarsen oxide.

Successful results have been reported in treating certain types of epilepsy with a new drug, *mesantoin*. *Tridione*, another new product, has continued to show favorable results in treating petit mal epilepsy.

Many allergy sufferers welcomed several new drugs which inhibit the action of histamine, which is released by the tissues in allergic reactions. Experimentation has proved the efficacy of two recent *anti-histaminic agents*, benadryl (β -dimethylaminoethyl benzhydryl ether hydrochloride) and pyribenzamine (*N*'-pyridyl-*N*'-benzyl-*N*-dimethylethylene diamine) hydrochloride. Patients with hives, skin allergy and serum sickness type of reactions caused by penicillin and sulfonamide drugs have gained

relief with these drugs. The isopropyl analog of epinephrine has been found to be an effective orally active bronchodilator and in clinical tests has shown promise in the treatment of asthma. In France, *Neo-Attergan* (*N*-*p*-methoxybenzyl-*N*-dimethylaminoethyl- α -aminopyridine hydrochloride) has been developed, and is undergoing clinical tests in this country.

Therapeutic applications have been developed for a number of compounds prepared and studied by the Chemical Warfare Service. Sulfur and nitrogen mustards, known as *contact vesicants*, were found to exert cytotoxic actions on various tissues. Experiments on transplanted lymphosarcoma in mice showed that dissolution of tumors could be rapidly effected when near-toxic doses were administered, but the growth invariably returned.

The program of the Chemical Warfare Service also developed di-isopropyl fluorophosphate (DFP) which has been used successfully in treating glaucoma and myasthenia gravis.

Radioactive isotopes for biological and physical tracer studies and for experimental therapeutic use were made available from the Oak Ridge uranium pile. This constructive application of atomic energy is beginning to be widely utilized and offers striking possibilities in the exploration and solution of the complex functioning of organic mechanisms and disease. Radioactive iodine has been successful in treating thyroid cancers and certain types of skin cancer have responded favorably to treatment with radioactive phosphorus.

N-propyl thiouracil has been found to be much more effective than thiouracil in the control of hyperthyroidism. Radioactive iodine is also valuable for this purpose as it is reported to remain concentrated chiefly in the thyroid gland, its beta-rays furnishing internal radiation similar to Roentgen radiation.

Clinical observations have indicated that *rutin*, a glucoside isolated from the green buckwheat plant, is effective in treating fragile and weakened capillaries and may be of use in

treating high blood pressure associated with increased capillary fragility.

Successful results were obtained in the immunization of monkeys with the first *mumps vaccine*. The vaccine is now reported to be in the final stages of development.

Experimental studies on animals have shown that *nutrition* can be a dominant factor in the incidence of spontaneous or induced tumors. Observations in dietary relationships have indicated that a low intake of choline of the vitamin B-complex could induce a high incidence of tumors in albino rats. It has also been found that a lack of milk in the daily diet of rats may influence the development of cancer of the liver.

BAL (2,3-dithiopropanol) developed by British scientists as an antidote to arsenical blister gases, is now available for civilian medical use in the treatment of arsenical poisoning. *BAL* (the term is a contraction for British Anti-Lewisite) acts in treating toxic encephalopathy, arsenical dermatitis and acute hyperpyrexia occurring as complications of arsenotherapy and in other types of heavy metal poisoning.

Reports on the development of *new drugs in Germany* were released during 1946 and investigations on them are being made in this country. Indications are that Amidone (1,1-diphenyl-1-dimethylaminoisopropyl-butanone-2), synthesized in Germany, is as active an analgetic as morphine. Several new drugs have been developed to relieve spasm of smooth muscle. In addition to Amethone which has been introduced commercially, β -diethylaminoethyl phenyl- α -thienylacetate hydrochloride, 1,1-diphenyl-3-piperidinopropane and others have shown promise in clinical tests in controlling spasms of the gastrointestinal tract.

Preliminary reports released from Russia on a new serum *KR*, secured from the blood of guinea pigs infected with the parasite of Chagas' disease, state that it may be effective in stopping growth of cancer cells and yet not harm normal cells.

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carrier state or to subdue purulent complications. Another culture was taken during the convalescent period after the sulfadiazine treatment. Cultures so obtained were tested by standard methods for sensitivity to sulfadiazine. None of the hemolytic streptococci, which were isolated following the course of sulfadiazine therapy, showed any evidence of having developed resistance to sulfadiazine. Apparently, therefore, the resistance that was observed among the troops during mass chemoprophylaxis was engendered by the use of small quantities of the sulfonamide over an extended period. When the drug is used for a brief period in large doses, as in Hartman's investigation, resistance probably is not encountered.

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PREGNANCY TESTS

A rapid chemical test for the diagnosis of pregnancy would be of tremendous clinical value. For a time the Guterman test, which was based on the color reaction of pregnandiol in urine, seemed to show promise. Recent reports, however, indicate that the test is not sufficiently reliable to warrant its widespread application.

Morrow and Benua found that a large percentage of normal nonpregnant women gave positive reactions during the luteal phase of the menstrual cycle. Furthermore, the test gave a negative finding in a normal patient seven weeks pregnant. They pointed out that when large amounts of seventeen-ketosteroids are in the urine, as in arrhenoblastoma, the test may be positive. Finally, if amenorrhoea exists without pregnancy and if the corpus luteum is functioning, a positive test may result. These findings have been corroborated in part by Reinhart and Barnes, who found that both positive and negative reports are subject to a 25 per cent error. They believe that the source of

error lies primarily in individual variations in the metabolism of progesterone in both pregnant and nonpregnant women.

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TANTALUM CRANIOPROSTHESIS

The discovery of the value of tantalum as a superior closure material for skull defects was a significant advance in surgery and brought to an end a search that had gone on for more than three hundred years. It is indeed a remarkable metal, biologically inert, malleable and ductile, yet stout enough so that a sheet 0.0125-inch thick protects the brain. It may be readily cut or worked at the operating table. Indeed, tantalum satisfied remarkably the exigencies of combat surgery, wherein the outstanding virtue of any technique or device (or man) is its adaptability to unpredictable circumstances.

During the war MacKay and Russell developed a "simple, easy, and quick method of repairing cranial defects from a basic, 'ready-made,' tantalum cranioprosthesis." Although the details of the operation itself cannot be treated here, mention may be made of the basis for their method. These investigators observed that most of the calvarium consists of a composite of segments of four spheroidal surfaces, centered around the four major prominences of the skull. The radii of these major surfaces all equal approximately $2\frac{1}{4}$ inches. These curved surfaces also constitute the only real problem of cranioprosthetics, as the intervening planispheric surfaces are easily duplicated. This being the case, the authors fabricate, by hammering, a tantalum hemisphere with a fixed radius, which serves as an exemplar from which one or several cranioprostheses of various specifications can be cut. This hemisphere is sterilized with the instruments at the beginning of the operation. In practice, the surgeon simply replaces one spheroidal surface of the skull with another identical one made of tantalum. Since these spheroids always have approximately the same curvature, the basic

exemplar of equal radius eliminates the necessity of molds, casts, or intermediate preparatory craniotomies. While MacKay and Russell do not believe their innovation to be the last word, they do report success with the method in the repair of twenty-five cranial defects. Interestingly, they observe that the South Sea Islanders hit upon a similar principle ages ago when they repaired cranial defects with coconut shell.

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STREPTOMYCIN AND TUBERCULOSIS

The veteran streptomycin investigators at the Mayo Clinic recently have reported their results with this antibiotic in the treatment of tuberculosis. One report is concerned with thirty patients with pulmonary tuberculosis to whom streptomycin was administered for two to six months. In general, the patients selected for investigation had tuberculosis that either was progressive or did not respond to bed rest. Streptomycin was administered, 1.0 to 4.0 gm. per day, in divided doses given intramuscularly or by deep subcutaneous injection every three to six hours. The evaluation of results was based upon changes noted in serial roentgenograms. Of twenty patients with far-advanced tuberculosis, nine showed marked and unexpected improvement, two showed moderate improvement, and five showed slight improvement. In four, no change was noted. Twenty-six of the total of thirty patients revealed some degree of improvement. In none did the condition become worse during the course of therapy. Exudative lesions showed the most rapid improvement. The changes evidenced roentgenologically were so prompt and consistent that there could be no reasonable doubt that the drug exerts a *suppressive* effect upon the disease.

Apparently favorable responses were obtained in a variety of extrapulmonary cases of tuberculosis. Here again, the drug appears to have suppressive value. All in all, the investigators view favorably the possibilities of streptomycin in the treatment of tuberculosis; but with laudable reservation they insist that the drug should not be used as a sub-

stitute for accepted and proved therapeutic procedures.

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UROLOGICAL CONDITIONS OF GILBERT ISLAND NATIVES

A physician in the Navy Medical Corps reports on urological conditions among the natives of the Gilbert Islands. Venereal disease is almost unknown among these islanders; such few cases as are found were caused by transient whites. Circumcision is commonly practiced and usually consists of a dorsal slit. Hydrocele is often seen. Sometimes it is of filarial origin, but more often is caused by scrotal trauma brought about by the heroic manner in which the natives climb coconut trees. Prostatic hypertrophy was observed in only one patient, a French priest!

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TOXIC REACTIONS TO DDT

Reports of toxic reactions to DDT continue to appear in the literature. Hill and Damiani report the case of a patient whose death apparently was caused by exposure to the fumes of a 6 per cent solution of DDT in kerosene with which the room in which the patient worked had been sprayed. The case is of particular interest because the authors state that the clinical, laboratory, and roentgenographic findings all were similar to those of periarteritis nodosa. Since other investigators have claimed that periarteritis nodosa is a hypersensitive state induced by such sensitizing drugs as the iodides and the sulfonamides, Hill and Damiani believe that DDT likewise should be included among the drugs producing effects that simulate this condition. The assumption is therefore made that DDT possesses allergenic properties that must be considered.

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Hill, W. R., and Damiani, C. R.: Death following exposure to DDT. *N. Eng. J. Med.*, 235:897, December 16, 1946.

R. W. C.

Consultation Service

We offer this special consultation information service as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from members of our editorial board best qualified to help. Each question will be answered by mail and answers of general interest will be published each month.

DUODENAL ULCERS

QUESTION: *Is protein hydrolysate useful in the treatment of selected cases of duodenal ulcer?*

Why does a common cold aggravate the symptoms of duodenal ulcer?

M. D.—Indiana

ANSWER: Casein hydrolysate or amino acid mixtures have been used in treatment of peptic ulcer with the assumption that general and local cell nutrition would be improved and consequently healing promoted. The indications for use of concentrated protein material would appear to be malnutrition or protein deficiency or when circumstances prevent giving adequate amounts of protein as food.

Systemic phenomena associated with an acute febrile infectious disease may activate a quiescent inflammatory condition of any organ. That is, changes in circulation, in body fluids, and in metabolism provoked by fever affect damaged tissue when normal cells are resistant. Transient bacteremia may be accessory to the other effects. The alterations at the site of a latent or healed peptic ulcer responsible for maceration or renewal of activity comprise hyperemia, probable congestion and edema, elimination of protective mucus, and possible inoculation by bacteria in the blood.

INFECTIOUS FEVERS

QUESTION: *When do the infectious fevers become infectious? For instance, is a child who is developing mumps liable to infect other children during the whole twenty-one days of the incubation period?*

M. D.—Kansas

ANSWER: Infectious fevers become contagious under different circumstances. In the case of mumps, the contagion begins at the time of swelling and continues until the swelling has disappeared. For those diseases that have a prodromal period, such as measles, the contagion begins with the onset of the prodromal symptoms, such as sneezing and coughing, and lasts until these symptoms have disappeared. The incubation period which is the time from exposure to the onset of the clinical symptoms is non-contagious.

OSTEO-ARTHRITIS OF LEFT HIP

QUESTION: *A male aged 70 has advanced osteo-arthritis of the left hip, which is painful and more or less fixed in partial flexion with marked adduction. Would subtrochanteric osteotomy, if successful mechanically, relieve or remove the pain, which is at present almost constant?*

M. D.—Missouri

ANSWER: If the physical condition of the patient is such that he can stand major surgery, the procedure of choice would probably be an arthrodesis of the hip of intra- and extra-articular type. The use of a long Smith-Peterson nail across the joint would probably decrease the necessary immobility. Subtrochanteric osteotomy and cup arthroplasty would be the next procedures to consider. The results with arthrodesis are usually the

most consistently good. If the patient is not considered a good surgical risk, one might try traction with Buck's extension and rest in bed for a few weeks followed by the use of crutches or a cane. Although this may give temporary relief, the chances of recurrence of pain and flexion deformity are great.

PENICILLIN REACTIONS

QUESTION: I recently had a patient to whom I gave penicillin throat lozenges (1 two-hourly for six days) for a streptococcal tonsillitis. The tonsillitis settled down at the end of a week but the patient's tongue became swollen and painful as if the superficial layer had peeled off. This healed in one week. The patient was not anemic. I concluded that the tongue condition was due to the penicillin. Would you kindly advise me on this?

M. D.—Michigan

ANSWER: In answer, let me state that throat lozenges and troches are all made up with calcium penicillin and that the hydrogen-ion concentration of calcium penicillin is a little on the acid side. This, therefore, should not cause the reaction described by the questioner. Rather, I believe that it is a localized allergic reaction of the tongue tissues to the penicillin. Similarly, use of penicillin in the eye will occasionally give rise to a contact dermatitis of the conjunctiva and lids.

PERNICIOUS ANEMIA

QUESTION: A man of 51 has had pernicious anemia for fifteen years, and for three years has received doses of liver extract. The symptoms of subacute combined degeneration have improved under treatment. His blood count is now five millions and his color index 1.16. Is it wise to continue with 4 ml. of liver extract weekly?

M. D.—Oklahoma

ANSWER: The proper maintenance dosage of an effective fraction of parenteral liver extract is that amount which prevents macrocytosis of the

erythrocytes and also the advance of neurologic symptoms. In general 15 units of liver extract injected intramuscularly at intervals of one to two weeks will accomplish this result.

EFFECTS OF STILBESTEROL

QUESTION: A woman of 51 had an erythematous condition of her face. A specialist prescribed 1 mg. stilbesterol daily for two months, then one month's rest. She now has uterine bleeding, though her menopause was three years ago, and she is worried about the possibility of pregnancy. Can I reassure her that stilbesterol does not cause ovulation after the menopause and that pregnancy cannot supervene?

M. D.—Illinois

ANSWER: Stilbesterol will not cause ovulation in a woman three years beyond menopause. This period of three years is taken to mean complete amenorrhea until the bleeding which was induced by stilbesterol through the formation of a hyperplastic endometrium. The likelihood of pregnancy in a woman three years beyond the onset of menopause will not be enhanced by giving stilbesterol.

ANGINA PECTORIS

QUESTION: What is the pathological condition in angina pectoris? What is the clinical distinction between angina pectoris and coronary thrombosis?

M. D.—Pennsylvania

ANSWER: Angina pectoris, usually referred to as a clinical entity, is a manifestation of coronary arteriosclerosis. It is due to the anoxemia of the heart muscle resulting from the insufficient coronary circulation because of the arteriosclerosis. Coronary thrombosis denotes a complete occlusion of a coronary artery, with the formation of a clot in the vessel and usually followed by infarction of the heart muscle. Angina pectoris occurs in this condition also, but the pain is more severe and of longer duration—usually more than one-half to one hour—than in coronary arteriosclerosis without occlusion.

Men of Medicine

Missionary To The Heathen

DR. ANTON J. "AJAX" CARLSON started out as a boy to be a missionary to the heathens. And he is still at it. At the age of 72 his definition of the word "heathen" has changed, but his spirit has not.

From his laboratory and office on the third floor of the Abbott Hall on the University of Chicago campus, where he is still carrying on research as Professor Emeritus of Physiology, he sallies forth on frequent missions to attack human ignorance and stupidity.

The songs and sermons of the old Swedish Lutheran Church whetted his zeal and ardor when, as a lonesome boy of seven, on the North Sea Coast, he herded sheep and watched the ships sail by for unknown ports.

He was born on a farm near Svarteberg—not far from Goteborg. His father died when he was five years old, leaving his mother with seven children and no money to support them. Anton, third from the youngest child, hired out to a neighboring farmer. But sheep-herding was no life for a vigorous youngster, and he says "the everlasting haa, haa, baa of the sheep" drove him wild. Deeply embedded was a strong desire for an education but, because of his circumstances, he knew it was impossible in Sweden.

The passing ships filled him with ideas. If he could get away to America, perhaps he could rid himself of this gnawing desire. He stuck it out until he was 17. His brother had gone to America, and Anton followed, to Chicago to take up carpentering. But his urge for an education remained strong, so after a year and a half at his trade, he entered Augustana College in Rock Island, Ill.

At Augustana he luxuriated in the religious zeal of the church and the community. He steeped himself in Latin, Greek, religious lore, and philosophy. But religion and philosophy did not rest too well on his mind and, when a professor of geology invited him to take part in studying a research problem—how the wind altered the contour of the earth—there was a reconversion.



Anton J. Carlson

"For the first time I realized that information is not just in books, that information in books is not always reliable," he says. "I read Greek, Greek, history, philosophy, blah, blah, blah, blah, blah."

Carlson stayed at Augustana to receive his bachelor and master of science degrees and then left for Stanford University to receive his doctorate in philosophy in biology. After his graduation with the doctorate he did research in biology for the Carnegie Institution in California, and then was sent to Woods Hole, the biologist's paradise.

Among biologists at that time there was a "Professor Emeritus of Physiology" who was known for his research on the reactions of the stomach to "Health and Disease," and the "Commission for the Advancement of Science."

controversy as to the origin of the heart beat. Did it start in the heart muscle or the nerves? The argument was something like the medieval controversy as to how many angels could stand on the point of the pin.

"Let's get the evidence," he said. He worked with the horseshoe crab as an experimental animal, and arrived at a verdict.

"It begins in the nerves," he said, "of the horseshoe crab."

Commenting on this guarded statement, he says, "Scientists must always look for the evidence, and examine the evidence critically to see if it is sound."

While he was enroute to Woods Hole, he met the late Professor G. N. Stewart, former head of the Department of Physiology at Chicago.

"I was in a saloon on Cottage Grove Avenue in Chicago (commonly frequented by University of Chicago faculty men) with some of my colleagues," Dr. Stewart related. "A brawny Swede breezed in.

"One of my associates hailed him with 'Hello, A. J.! Have you ever met Stewart?' 'No,' answered Carlson as we were introduced. I invited him to join us in some beer. He did, and I was greatly impressed with his capacity—both for beer and physiology."

Also impressed by his scientific method of attack in his Woods Hole research, Dr. Stewart invited him to join the Chicago faculty. He was appointed associate in physiology in 1904, assistant professor a year later, associate professor in 1909, and professor of physiology in 1914, when Dr. Stewart left for Western Reserve University.

In making his teaching dramatic and effective, Ajax would often pull out every stop. He could turn on and off his Swedish brogue at will—as he still does whenever he wants to create an effect.

He always lectured to college freshmen in physiology because he believed the "babes" should get the best start, and who could do any better than the head of the department himself?

When a student would offer as a fact something that created some doubt in his mind, Ajax would gaze at him, glasses propped on his forehead, and arms waving, would shout, "Vot iss de effidence?"

This caustic "Vot iss de effidence?" has made many a scientist cringe. Dr. Carlson has appeared in the audience of innumerable scientific gather-

ings, and it is said he has never fallen asleep at one of them. Although he has often been bored, he did not want any scientist to put anything over on him.

At one time Serge Voronoff was reporting on rejuvenation of humans through the grafting of monkey glands. Ajax sprang to his feet and shouted: "I knew of a case of a rejuvenated man in the United States who felt young until he received his doctor bill. Dot vos so high he suddenly felt old again."

Not only was Dr. Carlson critical of his students' method of thinking, but he was fiercely intolerant of laziness, tardiness, or any other sign of inattention or lack of interest. In the flapper days when a young woman student powdered her nose in the classroom, she was immediately told to get out. Tardy students would find the classroom doors locked. At one time, to pep up his students, he tried to hold classes at 6 o'clock in the morning, but that effort failed.

He was as fond of pranks as he was fond of being severe. One time he announced to a class that he was going to test their accuracy of observation. He placed on a table a glass of nauseous, vile-smelling liquid. He dipped in a finger, and put his finger in his mouth, without any change of facial expression.

"Now each of you will do exactly as I did," he directed. They all obeyed, and their faces contorted in violent distress.

They wondered how that damn Swede could take it.

"But," said Ajax, "you failed to observe that the finger I dipped in this solution was not the one I put in my mouth. Next time please observe more carefully."

He was as tough with his colleagues as he was with his students, and a temperamental, hard-driving worker.

Just back from Europe after World War I, where he had served with the Army, and subsequently the American Relief Administration, Dr. Carlson decided to do a series of investigations of the visceral sensory nervous system of lower animals. He recruited one of the younger men of the physiological faculty as his assistant.

After eating a hasty breakfast, they would get to work at 8 o'clock. They then would work without eating and without stopping until 3 o'clock the

next morning, snatch a bite of ham and eggs, sleep, and renew the ordeal the next day. This went on for weeks and months—Sundays and holidays included.

Neither Carlson nor his assistant would see their families for weeks on end. Carlson would not even carry on a conversation unless the subject applied to the work at hand.

From this experimental work Dr. Carlson and his assistant produced such a volume of reports that the editor of the journal to which they were submitted could not believe the two had actually done the work.

Shortly afterward the assistant in this research was given an assignment by the Rockefeller Foundation in Germany. There was still a volume of work to be done, but the temperamental Carlson's interest lagged. When anyone wanted to find him, he would be at the Quadrangle Club (Faculty Club) playing bridge during the day and most every night until 11 or 12 o'clock.

Dr. Carlson has been as outspoken with the administration of the University of Chicago as he has with his students, colleagues, and other fellow scientists. As a member of the American Association of University Professors, he has had many a set-to with the officers of the university. Taking part in a debate on the subject of freedom of teaching, he said, "So far as I am concerned, I don't look up to deans, nor do I look down on them. I just look at them."

When President Hutchins was new at the University, he proposed to eliminate all tenure privileges for the professors.

"I was at the meeting," Dr. Carlson relates. "President Hutchins argued that such a step would keep professors on their toes.

"'President Hutchins,' I said, 'aren't you slightly confused in your anatomy? What you mean is that it will not keep them on their toes. It will keep them on their knees.'"

President Hutchins' proposal didn't go through.

"But I get along with President Hutchins fairly well," Dr. Carlson says. "He doesn't understand science or the method of science. His face is toward the past. He is looking for the answers of the problems today in his 100 great books—but they are not there.

"The answers are in a better understanding of man instead of in emotions and traditions of the past."

Dr. Carlson says that America is scientifically illiterate. The method of science in education is neglected. People do not know how to scrutinize, analyze and improve the facts.

"Science in the schools and colleges is a quiz kid program," he says, "and in all mankind, the conditioned reflex toward the past is an iron chain that binds us."

In failing to apply the scientific method, Dr. Carlson says, educators drown children with facts, destroying their power to think.

"Young children have a wise stage—the age when they are everlastingly asking why that is so, and why this is so, and how this or that thing happens," Dr. Carlson says, "and we drown them with facts. The result is that we educate out of them their fund of mental curiosity with which they are born."

To get at the facts of human physiology, Dr. Carlson frequently uses himself as a guinea pig. He would starve himself for as long as five days to determine the reaction of his stomach in unusual situations. One day near the end of one of these periods of self-starvation, he had a cannula in his mouth, the end of which was held against the parotid duct to measure the amount of saliva flow. He had ordered a steak with mashed potatoes, gravy, and all the trimmings. Just as his assistant walked in with the feast and it caught Dr. Carlson's eye, the saliva squirted out through the cannula in a heavy stream.

Many times while doing his famous experiments on the motility of the stomach, he could be found in the laboratory with a tube with a condom on the end, down his esophagus, and inside his stomach recording the movements of that organ.

In those experiments he had a streak of luck, rare in the life of any scientist.

One of his colleagues discovered a harbor by the name of Fred Vleck, who in childhood had swallowed lye, which had closed his esophagus. To save his life, a surgeon had opened a window to his stomach so that Vleck chewed his food, and after he had obtained full satisfaction, spit it out into a tube that entered the stomach through the window.

After a drawn-out controversy with the University administration and the trustees, Dr. Carlson persuaded them to employ Vleck as a human guinea pig. He looked into the action of Vleck's stomach for 13 years until the man died of cancer of the esophagus, caused by the original burn.

Carlson fed him everything imaginable to find out how the stomach would react to it, from paraffine to whiskey. But the man was so nervous that everything Carlson did to him he had to do to himself in the man's presence.

He found that when the stomach is empty it begins to contract periodically, and that the contractions are not controlled by the brain or other portion of the central nervous system, and neither by sight, smell or taste of food.

A person may or may not be aware of the contractions of his stomach. Hunger, in fact, is distinct from appetite, which arises from the stimulation of the nerve endings of the mouth. There is, in a sense, he found, two forms of hunger—brain hunger and stomach hunger. These researches into the reactions of the stomach culminated in Dr. Carlson's greatest work, "Control of Hunger in Health and Disease."

In his work he came to the conclusion that periods of starvation of perhaps a week, were definitely good. His periods of fasting were as invigorating to him "as a month's vacation in the mountains," he said.

In somewhat different sense he believed the problem of feeding a hungry world is the number one problem that humanity faces.

This was impressed on him after World War I, when, as a member of the American Relief Administration, he visited all countries from the Adriatic to the continent of Asia.

"Every civilization in the past has gone under for failure to conserve the soil, and all species of animals tend to reproduce faster than the land will supply food to support them," he says. "Very soon the United States will need for itself all it can produce for an optimum of nutrition because of the increase in population and the waste of soil.

"We must think ahead, not 10 years, not 100 years, or 1,000 years, but 10,000, if the human species is to be saved from starvation. Ignorant

Americans turn up their noses at the Chinese, Dutch, and French peasants who put human night soil back into the land while we let it slip away from us into our rivers, lakes, and the oceans."

Probably more than any other American who saw Europe after World War I, he was privileged to see the "terrible backwash of the war"—the destitution, misery, and starvation. He was in Paris during the Versailles Conference, and said he was impressed "by the insincerity of Clemenceau, Lloyd George, and Orlando, who drew up the so-called peace."

"My conclusion was that war is an excellent preparation for the next war, and not a preparation for peace," he says.

This was his explanation of why, before Pearl Harbor, he took the platform for the America First Committee. He did not think American democracy could survive another war.

He did not hold with the Nazi ideals. Far from it. He believes that the human race is one, whether "white, black, yellow, brown, or tan." But, "it will take 10,000 years to work off racial prejudices, and by that time the whole species may be dead, as a result of our own stupidity."

During World War II he worked to the full extent of his time, energy, and ability in the service of such agencies as the Office of Price Administration and the Office of Scientific Research and Development. His latest project with the OSRD, which has been taken over by the National Academy of Sciences, is to find something better than the seeing eye dog as an aid to blinded soldiers.

He has served with the Federal Trade Commission, and for 30 years with the United States Food and Drug Administration, which he believes to be the finest of federal agencies. "When I am sure of my ground in fighting humbug and dangers in medicine, I go all out," he says.

In the last four years he has actively championed the cause of the makers of oleomargarine fortified with Vitamin A, against legislation limiting its use. He says the restrictive laws "touching the production, distribution, and consumption of margarine, are still in our statute books, and still render it more difficult for many people to secure adequate nutrition."

Dr. Carlson, as president of the Research Council

on the Problems of Alcohol, deplors the refusal of many doctors to treat alcoholics. He urges "an entire change in the social attitude and public understanding of the alcoholic problem" and points out that a recent survey of the facilities for treating alcoholism in New York City showed that fewer than 40 per cent of the doctors cared to handle alcoholic cases. "Yet, no matter how contemptible or how down-and-out a person may be who has contracted pneumonia, the medical profession would treat him."

He says that "as long as society looks on alcoholism as a sin, the doctor will look upon it as a moral issue and one that is outside his field. Perhaps a complete understanding of the causes of alcoholism would render this malady no more a sin than say, tuberculosis."

Ajax drinks and can take it strong—on occasion—and often to the amazement of colleagues with less steel in their sinews. But these occasions are not frequent.

He drinks primarily to relax, especially when he is at his cabin in Michigan, where he and his wife and family, as well as his colleagues and friends, make pleasure trips in the winter and summer. Using his talents as an ex-carpenter, which are equal to that of an excellent cabinet-maker, he built the original cabin. Mrs. Carlson, however, was not satisfied with it, so she had a log cabin built nearby. Dr. Carlson constructed the stairway, which is considered a fine piece of craft work.

He is uncanny as a woodcraft man. In the dead of the night he can find his way through the woods without a light or compass.

There is a tradition that Dr. Carlson is fond of breaking the ice and bathing in the cold water of the streams near his cabin.

The legend began when he was at the cabin with a guide and two of his staff members. The two slept upstairs, and he and the guide below. The guide snored so loudly that he couldn't sleep. Toward sunrise, he became impatient, bounded out of bed, stripped off his pajamas, and yelled at the startled sleepers above: "Anyone who can't do what I do is a sissy."

With a shout he ran out the door, and slammed it behind him. The shivering, sleepy men upstairs looked out through a crack in the cabin wall and

saw Ajax break the ice and wade in above his waist.

At another time his picture was taken with Dr. Andrew C. Ivy, famous Chicago physiologist and former student, standing waist-deep in icy water on a cold winter day. But he does not make a habit of too many frigid dips.

In full vigor of activity, rushing from one city to another on business, and from one speaking engagement to another, and alternating this with research problems as important as any he has ever undertaken, Dr. Carlson is a staunch defender of the worth of humans past the ordinary "retirement years."

"By keeping in idleness older workers who can still perform useful labor, we are not only wasting valuable human resources," he says, "but we are contributing to biological parasitism in, and degeneration of, human society. For man is no exception to the biological law that existence without effort, without struggle, impairs the species."

He still is interested in youth; and the possibilities of youth. He has taught young people for nearly 50 years and still spends some time in teaching.

"Certainly, I am interested in youth, for some day a teacher of freshmen will come face to face with a budding genius, perhaps even greater than Galen, Gallileo, Newton, or Pasteur," he says. "Teaching is always an exploration, an anticipation, a challenge, a joy, and never a drudgery."

He not only believes in the hope of youth; the usefulness of advanced age, but the need for greater education for adults, to clarify their thinking.

Dr. Carlson lives with Mrs. Carlson in a modest home not far from the University. He has two sons—Alvin, a surgeon in the Miami Valley Hospital in Dayton, Ohio, and Robert, in the advertising business in Chicago, and a daughter, Mrs. Alice Esther Hough. He has had numerous honors and has held important posts in many scientific, medical, and other societies. One of his more recent distinctions was that of 94th president of the American Association for the Advancement of Science.

He is living honestly and vigorously according to the full dictates of his conscience, seeking the truth, looking for the evidence, weighing and analyzing, discarding the untrue, and trying to make wishful thinkers, "softies," blind followers of tradition, and other "heathens" see the light.

Book of the Month—A Report

AN INTEGRATED PRACTICE OF MEDICINE*

A Synthesis of the Present Material of Everyday Practice

SUCCESS of clinical medicine requires appreciation of the unique character of the individual plus comprehension of his ailment and the reaction of his body to it. These prerequisites cannot be realized from application of rigid rules. Medicine is not an exact science, but rather a subtle combination of elements in which knowledge is subjected to the full play of intuition and imagination. Efficacy of a therapeutic program is determined, first, by exactness of diagnosis, and second, by the understanding skill with which the medical arts and sciences are incorporated into a regimen for the particular patient. In conditions such as scarlet fever, rheumatic fever and tuberculosis, for instance, responsibilities extend beyond termination of the acute phases of disease to projection of psychic, emotional, social, and economic consequences and preparation of the patient for necessary adjustments.

Mechanisms of the body are complex and the extent of medical knowledge vast. No man can hope for complete mastery of either in all their ramifications. As a practical matter in many situations, the best he can do is to know where to turn for the information he wants at a given time. Yet every physician who has sought guidance from books has been bogged down at some time by the lack of order in medical literature. Perhaps he has even sworn to himself that when he had the leisure he would attempt to coordinate and systematize

the particular field of his special interest. Others have felt the same way.

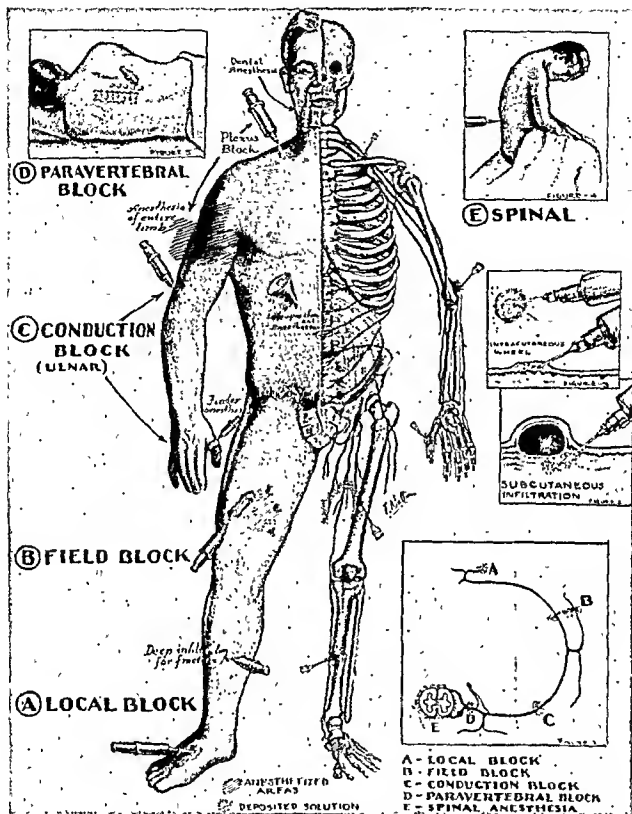
From time to time physicians have attempted to bring order out of chaos. Two notable coordinators were French and Cabot. But as recently as last year the Commonwealth Fund reported that:

No short-cut to the integration of specialized knowledge into comprehensive medical care has yet been devised, but until this problem is solved medicine—and therefore training for medicine—will be inadequate.

This twofold inadequacy is emphasized by the trend towards the extremes of specialization, a trend that is accelerated by both the complexity and the volume of medical knowledge. If a man cannot master the whole, perhaps he can assimilate a part. That is the great advantage of specialization. The dangers are impairment of the doctor-patient relationship and actual deterioration in medical care. The patient may no longer entrust the matter of his health to a single practitioner, but in effect, become his own diagnostician, choose the specialist to treat the ailment which the patient decides he has. On the other hand, there may be a tendency for the patient to lose his identity as an individual in the eyes of the physician and be looked upon as a case of this or that.

In the teaching and publishing fields, at least, are indications that the trend towards overspecialization has reached its peak. During the next decade, young doctors specializing in various branches of medicine may be forced into more general types of practice by the increasing demand for the family physician. Dr. Harold T. Hyman and the W. B.

*An Integrated Practice of Medicine. A complete general practice of medicine from differential diagnosis by presenting symptoms to specific management of the patient. By Harold Thomas Hyman, M.D. Four volumes and Index. 1,184 illustrations. 4,336 pages. W. B. Saunders Co., Philadelphia. 1947. \$50.00.



Illustrations from Hyman: *An Integrated Practice of Medicine*

Nerve block, a study of basic methods. Showing on the two sites of the body the surface appearance and anesthetized areas and the course of the nerves and actual site of deposit of the anesthetic solution.

Saunders Company must have had these men particularly in mind when they laid out the broad outline of *An Integrated Practice of Medicine*. The appeal of the four-volume set is to general practitioners to whom it is dedicated, and to the specialists desiring a ready reference to other fields.

Dr. Hyman is an internist in New York City, and an associate Professor of Pharmacology at Columbia University College of Physicians and

Surgeons. He has gathered about him a group of well-qualified New York practitioners and specialists to collaborate in this ambitious program of integration of medical knowledge. The volumes are made up of 25 sections, each devoted to a clinical specialty. In general each section was written by a general practitioner, a specialist, and Dr. Hyman. The authors have not attempted a catalogue of recommended remedial agencies or

technics, but have expressed personal opinions concerning the usefulness or uselessness of various methods of therapy. On controversial matters universal agreement is not expected and Dr. Hyman invites correspondence from readers who maintain opinions opposite to those expressed in the book.

The sections of the book are grouped somewhat heterodoxically under five headings: (1) Bodily injuries and bodily responses to injury, (2) Disturbances of the systems of communication and coordination, (3) Disturbances of end organ systems, (4) The technics of medical diagnosis and therapy, and (5) Prognosis.

The first heading comprises six sections: (1) General reactions of bodily tissues, (2) Infection, (3) Allergy, (4) Neoplasms, (5) Disturbances of metabolism, and (6) Poisoning.

The second heading includes (1) The circulatory system, (2) The Blood and blood-forming organs, (3) The organs of internal secretion, (4) The Nervous system, and (5) The eye.

The third heading covers (1) Digestive system, (2) Respiratory system, (3) Urinary system, (4) Male reproductive system, (5) Female reproductive system, (6) Obstetrics, (7) Pediatrics, (8) Skeletal and locomotor systems, and (9) Tegumentary system.

Under the fourth heading are grouped (1) Physical diagnosis, (2) Laboratory methods, (3) Medical therapeutics including pharmacotherapy, and (4) Surgical therapeutics. The fifth heading is devoted entirely to the art of prognosis.

Each section is prefaced with a brief discussion of the involved anatomy and physiology. For the most part pathology is given in bare outline. In many sections, when the subject matter is inexorably linked with normal function, pathologic physiology is included in the introductory chapter. The topic of uremia, for instance, appears in the first chapter of the section on the urinary system. Discussions of various diseases proceed along fairly common lines.

The second element in each section is a discussion of the special methods of and examination peculiar to the specialty or system under consideration. In the description of clinical manifestations of disease, emphasis is on asymptomatic stages and early symptoms and signs. In the symptomatic

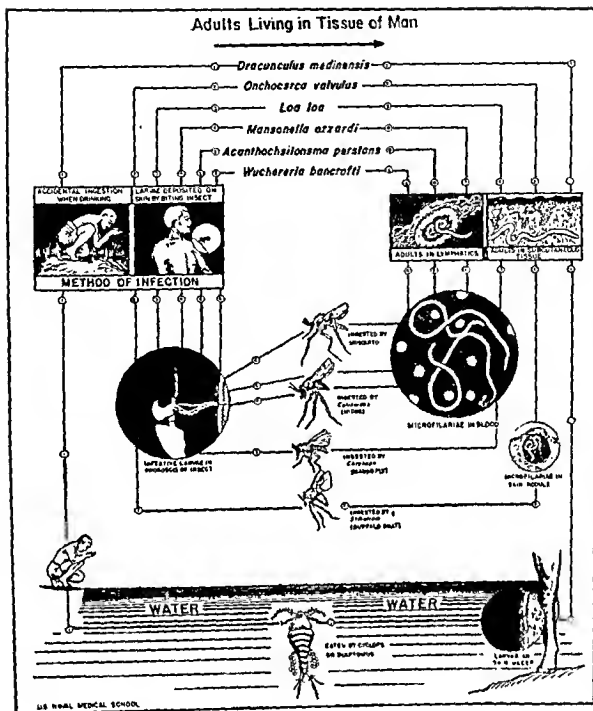
phases, the accent is on herald manifestations, such as Koplik spots and hyperemia of the nasopharynx and conjunctiva, which occur in measles, a day or so before cutaneous eruption. Apparatus and solutions necessary for performance of routine laboratory tests are given, together with steps in the procedure and guides in interpretation.

The closing portion of each presentation is devoted to therapeutics. Prophylactic measures, specific treatment and symptomatic therapy are all taken up for each entity. Technics of therapy are summarized or given in detail in the final volume. When specific therapy is utilized for a single purpose, details are transferred to the section devoted to that subject. Thus the material on anti-infective agents appears in the section on infection; digitalis and quinidine are dealt with in the section on circulatory diseases.

An Integrated Practice occupies an intermediate position between a single medical text and the voluminous encyclopedia. There is no exact counterpart in recent medical literature. The outstanding distinguishing feature is the differential diagnosis tables. The editor has attempted to delineate the problem to the reader as a patient would to his physician. Until the significance of a presenting symptom or sign has been interpreted there is no basis for therapy or prognosis. An immense amount of labor has gone into the production of differential diagnostic tables illustrating many symptoms and signs. These tables alone are worthy of collection and separate publication. Whenever possible individual signs and symptoms, especially symptoms presenting complaints, are isolated and the differential diagnosis is given in tabular form. In general each table is placed with the clinical condition with which the symptom or sign is most commonly associated; for example, the differential diagnosis of headache appears with Migraine.

The tables are confined to two columns, the left-hand column listing the possible causes for production of the symptom, and the right-hand column containing a telegraphic description of clinical manifestations and diagnostic features, together with suggestions for further investigations leading to a definitive recognition of the specific disorder.

After elicitation of positive findings the tables permit diagnostic possibilities to be narrowed down



Life cycles of important human roundworms.

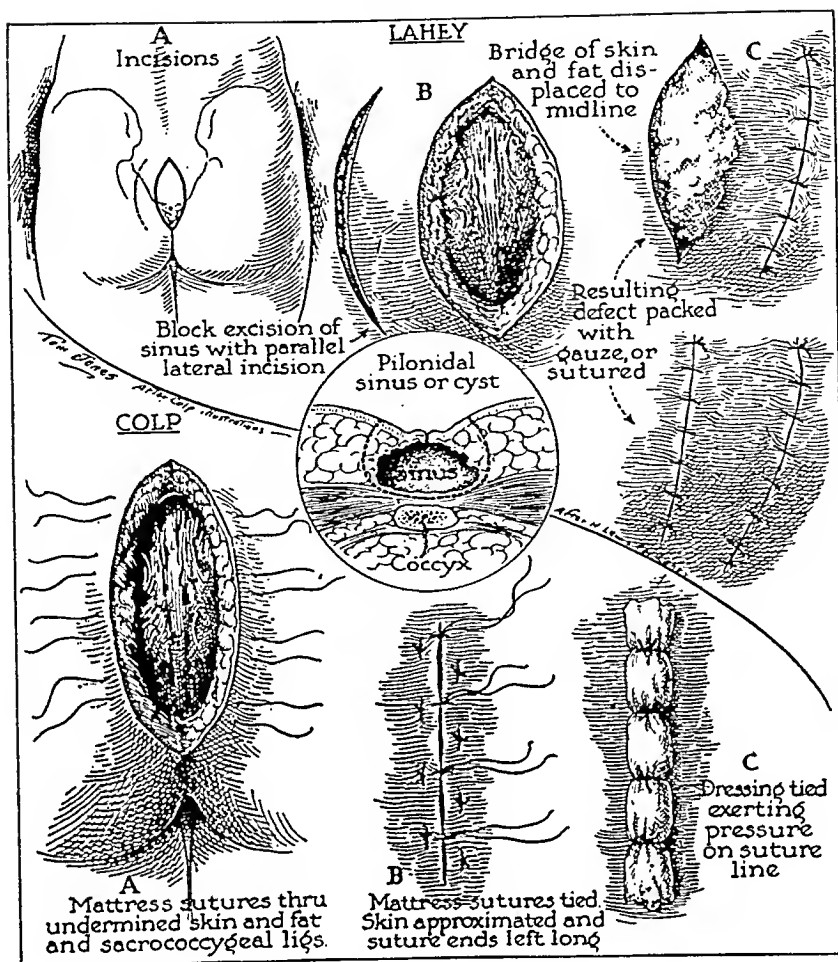
to a few subjects. When diagnosis has been defined page references lead to material which provides guidance toward prognosis and a therapeutic program.

Since a set of this type is intended primarily as a work of reference the accessibility of the material is important. In *An Integrated Practice* the integration is accomplished by the tables of differential diagnosis, by the cross references which appear throughout the text, and by the context which emphasizes, in each separate presentation, the broad systemic consequences of local disturbances as well as local manifestations of systemic disease.

The books are well indexed, each volume indi-

vidually and all collectively. A separate desk index, really a fifth volume, is included with the set. This fifth volume, in addition to a general index, contains a special index of differential diagnosis so that any particular symptom or sign may be located rapidly. Thus the publishers have sought to facilitate finding answers in the book for whatever questions the physician may have in mind.

In his preface Dr. Hyman states his cardinal aims as (1) delineation of the broad fields of general practice, (2) arrangement of material in the chronologic sequence of everyday practice, and (3) integration of the various subjects so that each discussion focuses consideration of the human



Operative treatment of pilonidal sinus.

being as a biologic entity. The work was attempted, he says, to "correlate the clinical aspects of the practice of medicine for medical students, internes, younger practitioners of medicine, physicians who have been diverted from civilian to military practice, and for those who have spent their lives caring for home communities. It is the hope that tangible data obtained from the basic sciences may have been thoroughly fused with the broader physiologic, economic, sociologic, and humanitarian aspects of the doctor-patient relationship."

These aims are laudable, but in attempting to integrate all of medicine Dr. Hyman sometimes falls into the same pitfalls that have entrapped his predecessors, oversimplification and a condensation so rigorous that only generalities remain. That he

falls short of his goal is no discredit. The integration of medicine is something scarcely to be accomplished by a book or series of books.

An Integrated Practice does, however, force attention to the fact that there are multiple causes of bodily reactions. It may suggest a line of investigation to follow in elucidation of obscure symptoms.

This is an altogether new postwar text. The material is abreast of the times although it is still too soon to expect proper evaluation of the contributions of war medicine. The work of Dr. Hyman and his collaborators represents in its own way a swing of the pendulum from specialization. It truly considers the patient as a whole.

What Other Editors Think

Editorial Evaluations of Current Contributions to Medical Progress

BLOOD PRESSURE AND AGE

IT is important to interpret correctly the significance of blood pressure findings in individuals over fifty. If the physician has the opinion that the normal blood pressure in this age group is the same as in the younger group, he will label those with moderate elevation as pathological and may cause the patient needless concern.

Two points of view as to normal blood pressure in advancing age have been expressed: one, that it is the same as in youth, and the other, that it tends to increase with years. A rather general view is that a person is entitled to a systolic blood pressure of 100 plus his age. Is this correct?

An article by Russek and Zohman, in reporting the results of blood pressure readings on 3,691 men between the ages of fifty and ninety-five, confirms other reports that the systolic blood pressure does increase with age, whereas the diastolic remains about constant. Their figures show an increase in systolic pressures from 138.9, on an average, for the fifty to fifty-four age group, to 164 for the eighty-five to ninety-five group. The average diastolic readings, however, remained around 87 to 90 in all the groups over fifty years of age.

It is reasonable to explain these findings, partly at least, as due to the loss of elasticity in the aorta. It is the elasticity of the arteries, of the aorta particularly, that maintains blood pressure during diastole. Any appreciable loss of this elasticity would tend to a lowering of diastolic pressure, and a compensatory increase in systolic pressure to maintain normal physiologic circulation, would be expected.

If normal blood pressure readings are the average obtained in the examination of large groups of presumably normal individuals, then we may conclude that systolic pressures ranging from 140 in individuals fifty years of age, to 164 in those over

eighty-five, can be considered normal, and, roughly, an individual is entitled to a pressure of 100 plus his age.

Minnesota Medicine, Vol. 29, P. 1253

SYPHILIS AND PENICILLIN

IN THE COURSE of penicillin therapy, problems arise in connection with the penicillin-resistant case and in matters of relapse, reinfection and reactions. Public health aspects, including the question of the returning veteran and marriage, are topics of concern in connection with penicillin therapy. These and other matters must be carefully considered, especially in the light of the gradually increased dosage of penicillin that is being recommended from time to time following careful studies of treated cases. Some of these patients did not receive enough penicillin to cure their syphilis and have relapsed or will relapse.

The matter of relapse is of special significance. In the group of clinics sponsored by the National Research Council and the United States Public Health Service the cumulative percentage failure at the end of eleven months after treatment varied from 15 per cent with a dosage of 2,400,000 units of penicillin to 62 per cent with one of 600,000 units. About 10 per cent of these failures were actually due to reinfection, but the rest were relapses. Various treatment schedules were used in the different co-operating clinics and in general it can be said that there were fewer failures when both arsenic and bismuth were used in combination with the penicillin.

Another complication has been added by the changing character of commercial penicillin. Various fractions of penicillin have been found and designated G, X, F, and K. Penicillin K is relatively inefficacious, since it is rapidly destroyed in the body; this assumes significance because of the fact

that certain commercial penicillins have recently shown an increasing content of penicillin K. It is also not known as yet whether increasing purification of penicillin removes some of the substances that have great therapeutic activity.

As a result of reviewing these cases in the various cooperating clinics it has been suggested that for seronegative primary syphilis the minimum dose of the at-present-available penicillin should not be less than 3,600,000 units, given intramuscularly in doses of 40,000 to 60,000 units at two-hour or three-hour intervals. For seropositive and early secondary syphilis a dose of not less than 5,400,000 units is recommended. If a relapse occurs, arsenic and bismuth should also be given when the course of penicillin is repeated. Penicillin by mouth is not advocated. Thus, the treatment of syphilis by penicillin has repeatedly been modified as further study of treated cases has progressed.

Emphasis is placed on the fact that the present recommendations are only tentative and are subject to revision as the results of treatment are further studied. The eventual value of penicillin in syphilis is still uncertain, and its ultimate status will not be established for several years to come. To be sure that syphilis has been successfully treated by any new procedure requires a long period of observation, measured in terms of years, not months. Every physician thus has a particular responsibility for the careful follow-up, serologic and clinical, over a period of years of every penicillin-treated case of syphilis that he sees, whether the penicillin was received in civilian life or during military service.

*The New England Journal of
Medicine, Vol. 235, P. 952*

INFECTIOUS LYMPHOCYTOSIS

IN 1941 Smith in America drew attention to a benign and probably infectious lymphocytosis appearing as an acute or chronic disease in children. The acute cases had a vague and varied symptomatology, but a sharp lymphocytosis was always present. The chronic cases usually followed an infection of the upper respiratory tract; there was a low, persistent pyrexia, vague malaise and anorexia, and often spasms of peri-umbilical pain;

a persistent lymphocytosis lasted a month or more; eventually the whole disturbance settled down, and there were no complications.

Duncan described an acute case in a girl of five years, beginning with acute abdominal pain and rigidity; there was no enlargement of lymphatic glands, liver, or spleen; there were 29,600 lymphocytes per c.mm., sternal puncture showed increased cellularity with 86 per cent lymphocytes, platelets were rather low, but red cells and hemoglobin were normal; the Paul-Bunnell (heterophile antibody) reaction was not significant. The acute symptoms subsided in a few days, but the pyrexia and the lymphocytosis persisted for a month. Later Duncan reported two cases in young adults, and added a morbilliform rash to the clinical picture.

Lorenz and colleagues report two more cases in children with peak counts of 47,500 and 58,000 lymphocytes per c.mm., and clinically only mild respiratory affection; sternal marrow was normal in these patients, with no lymphocytosis; the Paul-Bunnell reaction was positive up to a titer of one in eighty, but this is too low for a diagnosis of infectious mononucleosis. Steigman reports an outbreak which involved six children in one village in southern England; here cervical lymph-glands were notably enlarged and there was protracted lymphocytosis, but all recovered without incident. Smith says the disease is contagious and infectious, with an incubation period of twelve to twenty-one days.

There are already several known causes of lymphocytosis in children. Kato pointed out that from three months to four years of age lymphocytes are normally more numerous than polymorphs. A well-marked lymphocytosis has been recorded in whooping-cough, rubella, and mumps after the initial stage. Infectious mononucleosis is common in children, and it is likely that several cases of infectious lymphocytosis have been classified with this disease—for example, Thelander and Shaw's cases of infectious mononucleosis with signs of meningeal irritation, which had a lymphocytosis and negative Paul-Bunnell tests.

Here, then, is a benign almost certainly infectious condition, mainly affecting children, with a very variable clinical picture, sometimes simulating acute abdominal or nervous disease at onset; and sometimes only a mild respiratory tract affection;

pyrexia may be protracted and the blood shows a pronounced lymphocytosis. The Paul-Bunnell reaction is not significant. The differential diagnosis from infectious mononucleosis (glandular fever) may turn on the Paul-Bunnell reaction—not an entirely reliable sign—but the blood picture in infectious lymphocytosis shows only small lymphocytes, with no glandular fever cells or excess of monocytes. In lymphatic leukemia the patient is much more ill and has a rapidly increasing anemia, and sternal puncture always shows a massive lymphocytic infiltration.

The prognosis in infectious lymphocytosis is excellent, even if the course is long; no specific treatment has been proposed. The cause has not been identified; it has, as usual, been ascribed to a virus, but no supporting evidence has appeared yet.

The Lancet, Vol. 251, P. 949

FOLIC ACID

THE INTRODUCTION of folic acid constitutes one of the most important therapeutic advances of the past year. This substance is the latest addition to the growing family of the vitamin B-complex group and, because of the many conditions in which it has already been found to be of value, it seems probable that it may become more widely used than any of its close relatives.

Indications—It has been shown that folic acid is very closely allied to, if not identical with, the red cell maturation factor long known to have been present in liver extract and yeast. It has been found to be highly effective when given either orally or parenterally in inducing remissions in sprue, celiac disease, pernicious anemia and other macrocytic anemias.

Whether or not folic acid will supplant liver extract as the primary therapeutic weapon in pernicious anemia is not known. It has been found that remissions which are characterized by a reticulocyte response and an increase in red and white blood counts, platelets, and hematocrit values occur regularly following the daily oral administration

of a few milligrams of folic acid to patients with pernicious anemia in relapse. Whether or not complete remissions can be maintained indefinitely by continuing this therapy or whether or not the neurological disturbances often associated with pernicious anemia can be satisfactorily controlled by folic acid therapy awaits further study. For the present it seems best to combine parenteral liver extract with folic acid therapy in all cases of pernicious anemia associated with postero-lateral sclerosis.

In sprue and celiac disease the daily oral or parenteral administration of folic acid is attended by a rapid improvement in appetite, by a decrease in the number and bulk of the stools, and by a return of the blood picture to normal. The results are superior to those obtained by the use of liver extracts and special diets. It is important, however, that an adequate diet be given. Small doses of folic acid given daily probably are necessary to prevent recurrences in these patients.

In the macrocytic anemias associated with nutritional diseases (pellagra), pregnancy, liver disease (cirrhosis) and those which may follow gastric resection, folic acid has been shown to be highly effective, the results being better than those following liver extract therapy. Best results are obtained when the drug is given intravenously.

Dosage—The final word on ideal dosage of folic acid cannot be stated at this time. In treating pernicious anemia, 10 to 20 mg. given daily in divided doses by mouth seem sufficient to induce remissions in nearly all cases. Following return of the blood to normal, 5 mg. daily is probably a large enough dose to prevent relapse. Similar doses are indicated in sprue and celiac disease. When parenteral therapy is indicated, 1-5 mg. are given intravenously or intramuscularly once or twice daily.

Toxic effects—Unpleasant side effects are encountered rarely when the doses mentioned are given. Gastrointestinal upsets may occur, but are usually controlled by a reduction in dosage. When the drug is given intravenously the usual precautions of such procedures must be observed.

Bulletin of the New England Medical Center,
Vol. 3, P. 274.

New Drugs

The information in this department has been supplied to Postgraduate Medicine by the manufacturers of the products described.

GELFOAM, NO. 12, STERILE

PURPOSE: To provide hemostasis in neurosurgery, otolaryngology, bone surgery, malignancy, abdominal surgery, and proctology.

DESCRIPTION: Gelfoam is prepared from a non-antigenic, specially treated gelatin solution which is processed to give the desired porosity, dried, sectioned and sterilized.

INDICATIONS FOR USE: Soak gelfoam in sterile saline or thrombin solution and apply to bleeding area. Gelfoam is completely absorbed in about four weeks when implanted in tissues and does not cause excessive scar tissue formation.

HOW SUPPLIED: In jars containing four sterile sponges each having a surface area of 12 square centimeters.

PRODUCER: The Upjohn Company, Kalamazoo, Mich.

OENETHYL HYDROCHLORIDE

PURPOSE: Vasopressor substance for spinal anesthesia.

COMPOSITION: 2-methylaminoheptane.

DESCRIPTION: An aliphatic amine. A colorless, volatile fluid, slightly soluble in water which combines with acids to form salts which are readily soluble in water.

INDICATIONS FOR USE: Oenethyl hydrochloride is a vasoconstrictor having a pressor effect indicated in spinal anesthesia to raise a depressed blood pressure. Therapeutic doses of Oenethyl rarely cause undesirable side effects, such as nervousness, palpitation, headache, and dizziness. Oenethyl is indicated only in combatting hypotension brought about by spinal anesthetic.

DOSAGE: Intravenously or intramuscularly in doses of 1 cc. (50 mg.) divided in doses of 5 to 10 mg. (0.1 cc. to 0.2 cc.) at 15- to 30-second intervals with continuous check on changes in blood pressure. Whether intravenous or intramuscular route is used is dependent upon the depth of fall of the blood pressure and urgency of the case.

HOW SUPPLIED: Ampules of 1 cc. each containing 50

mg. ($\frac{3}{4}$ grain) 2-methylaminoheptane hydrochloride in boxes of 6 and 100.

PRODUCER: Bilhuber-Knoll Corp., Orange, N. J.

ALCO-DEX

PURPOSE: A substitute for morphine in the relief of post-operative pain.

COMPOSITION:

Alcohol	5 per cent
Dextrose in saline with Vitadex	5 per cent
Thiamin chloride	3 mg.
Riboflavin	4.5 mg.
Nicotinamide	30 mg.
Pyroxidine hydrochloride	3 mg.

DESCRIPTION: An intravenous solution which relieves postoperative pain and supplies food, salt, and fluids to the patient's system. The action of Alco-Dex is slower than morphine, but it is non-habit forming and does not cause constipation or postoperative distention. The alcohol tends to increase the respiratory rate and in this way has a protective action against pulmonary complications which may follow surgery. Alco-Dex is a source of calories and contains sufficient amounts of B-complex to counteract the deficiency of those vitamins caused by carbohydrates and alcohol.

INDICATIONS FOR USE: As soon as the postoperative patient feels any pain.

DOSAGE: Suggested rate of administration would be 50-70 drops per minute, approximately 200-250 cc. of 5 per cent solution per hour, depending upon the tolerance of the patient.

CAUTIONS: Because the action of alcohol as an analgesic is slower than morphine, even though more prolonged, it is suggested that medication be started as soon as the patient feels any pain rather than waiting until pain is acute as sometimes is done in the use of morphine.

HOW SUPPLIED: Available in four different combinations in liter flasks.

PRICE:

	1-7 Cases	8 Cases or More
Alcohol 5% with Vitadex B in D-5-S.....	1.65	1.50
Alcohol 10% with Vitadex B in D-5-S.....	2.20	2.05
Alcohol 5% with Vitadex B in D-5-W.....	1.60	1.45
Alcohol 10% with Vitadex B in D-5-W.....	2.15	2.00

PRODUCERS: Cutter Laboratories, Berkeley, Cal.

After Office Hours

We have been impressed by the appeal of a large insurance company for everyone to engage in a hobby—any hobby. This organization says that having a hobby will add years to a person's life and we are of the same opinion.

We have heard doctors say that all men, especially in the medical profession, need subordinate avocations. John Fallon, surgeon of Worcester, Massachusetts, has occupied his spare moments by collecting *Medica Litteraria*—poems, novels, philosophies, plays, and essays. His collection may be favorably compared to those of Mayo, Holmes, Osler, or Cushing. His home is a storehouse of medical ineunabula.

We cornered Doctor Fallon at a recent American College of Surgeons meeting and asked him to tell us more about his hobby. Being something of a poet himself, he talked about doctors and poetry. "Some doctors have put out their verse from behind false mustaches or pseudonyms, perhaps because of the opinion that poets are irresponsible fellows. If you had, say pneumonia, and suddenly found that your doctor, that strong quiet man between you and death, was writing an 'Ode to a Robin,' wouldn't your confidence go down and your temperature go up?"

"Yet," continued Doctor Fallon, warming up to his favorite topic, "there is a fundamental kinship between the doctor and the poet. True, medicine is keeping calm, knowing hooksful of facts and figures, listening pa-

tiently, deciding coldly and poetry is sky-rockets and explosions. Medicine is snuffy noses and lumbago; poetry is visions. But medicine is essentially sympathy, the desire to help a fellow man in sorrow, need and sickness. And so is poetry. The poet is the doctor of the sick soul: he makes them believe, and hope, and go on. And there are two other bonds between the doctor and the poet: both of them neglect their families for their work and forget their fees."

* * *

One doctor who was past seventy when someone suggested book-collecting to him, stated that this interest had added ten years to his life by providing zest to his days.

* * *

Music offers one of the finest means of relaxing and the best musical relaxation of all is to *make* music, not listen to it; to sing in a chorus or to play something, preferably with a group. Action, self controlled, a psychologist will tell you, is the solution for all kinds of fears and tensions.

Doctors who wouldn't live in New York if we gave them the place are seriously advised to reconsider their pronunciamiento. They would have difficulty recognizing the town around Irving Place at Eighteenth Street. While keen-eyed observers probably suspect the worst, weekly rehearsals of the Doctors' Orchestral So-

cietty of New York are held every Thursday at the National Hospital for Speech Disorders.

According to reports in a recent *New Yorker*, the orchestral society has been active since 1938 and includes several dozen medical men about town. Of a Thursday night one is apt to see and hear Dr. William Spielberg, a nose-and-throat and violin specialist; Dr. Charles Auer, internist-flutist; Dr. Sidney Robbini, dermatologist-violinist; Dr. Charles Gottlieb, x-rays and viola; Dr. Ricardo Gorbea, obstetrics and oboe; Dr. Abe Salzman, pathology and bass fiddle; Dr. Charles Gardner, dentist-violist, and Dr. Alexander Sved, orthodontist-violist. The president of the society is Dr. Cornelius H. Traeger, a diagnostician who specializes in arthritis and the bass fiddle. With the income from annual dues of \$25.00, the society has bought an extensive library of arrangements and pays for the services of a non-medical conductor.

For public performances, the orchestra is augmented by a few non-medicos, and even at rehearsals a handful of ringers play—a second-violin lawyer for instance, who takes care of the society's few legal matters. Because of the unpredictable nature of their profession the doctors do not know what kind of an orchestra may be assembled on any particular night. One Thursday, six clarinetists and only two cellists will show up; the following week there'll be two clarinetists and eight cellists. The society is looking for

a harpist and could use two French horns, an English horn, and a bass trombone.

* * *

One doctor we know whose hobby is collecting old insurance blanks which are found among reports to the British and American medical journals, has a lot of fun with a collection such as the following:

Mother died in infancy.

Father went to bed feeling well and next morning woke up dead.

Applicant has never had a fatal illness.

Grandfather died from gunshot wound caused by an arrow shot by an Indian.

Father died, suddenly—nothing serious.

Mother's last illness was chronic rheumatism but she was cured before she died.

* * *

Dr. Carl Binger of Cornell University Medical College has charged that the incessant "hammering" of radio commercial plugs to make listeners brand-conscious has become a serious source of medical misinformation. Dr. Binger also lashed out against Hollywood's pseudo-psychiatric motion pictures.

The doctor who, say, has sixteen years of medical education with ten years of specialization in psychotherapy, is caught flat-footed because he can not understand the vernacular his patients have acquired from the movies. Gordon Kahn, Hollywood specialist on the subject, suggests that the following might happen to any old fashioned doctor who has not kept up with movie versions of psychiatric methods:

"Ah, dreams," probes the doctor.

"And the only way I can describe them is in simple layman's language. They're anagogic.

ic. Anagogic as all get out."

The doctor defrosts. He thinks here is a simple fellow who has picked up a few random professional phrases while shopping around for treatment. And now, By Messmer!—he'll get it. "I might suggest a trial analysis."

"Where have you been, Doc? Why that technique went out with 'Lady in the Dark'—you know where Ginger Rogers goes off into a lot of yacketyack there on the couch."

"Just to fix a point of departure."

"Frame of reference, you mean."

"Precisely, by free association—"

"Are you kidding, Doc? That stuff was all right in 'Spellbound,' where Bergman and that little Russian analyst had Gregory Peck on the ropes. Put old Freud back on the shelf along with Charcot."

"But Freud discovered—"

"And so did Columbus. But you wouldn't think of using his maps now! What about Selznick and Zanuck—" The patient himself is a busy man. He wants to catch "The Spiral Staircase" and "The Blue Dahlia" before the night prices go on.

"I'll go in for narcosis," he says, "the way Doc Larsen gave it to Ann Todd in 'The Seventh Veil.' Just hit me lightly with one cubic centimeter of pentothal intramuscularly, and in a couple of minutes I'll open up like fourth-class mail."

And no reaching for that crock of insulin, either, Doc. This man is hep. He's seen the movie "Shock." Twice he's seen it! He knows what a psychiatrist is likely to do with a hypo of insulin.

* * *

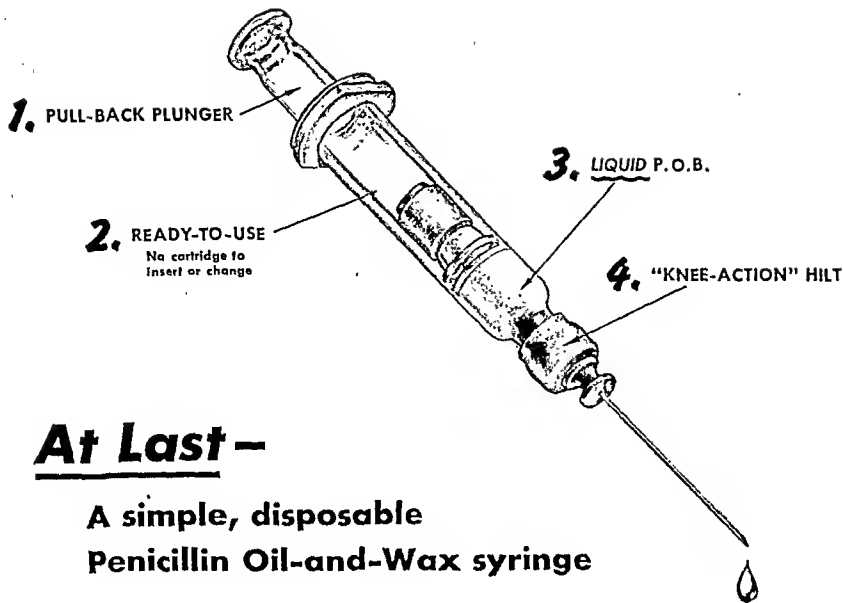
A letter from Charles Brown of San Antonio, Texas, gives us the news that the Naylor Com-

pany of that city is about to publish his book, *Bars from Bilibid Prison*. Doctor Brown, who has had thirteen years of active service in the Army Medical Corps, tells us that this collection of more than one hundred poems was written during his three years' captivity in Bilibid prison following the fall of Bataan. The poems are printed as they were originally written on scraps of paper and not a line or a word has been changed. Here is the philosophy of a prisoner—of all prisoners—of all times.

Doctor Brown says: "If you will bear with me, I would like to tell you a little about it. I have arranged the poems in four sections with an explanatory text that is an attempt on my part to tell briefly: (1) the history of the Spanish prison Bilibid, (2) the siege of Bataan and Corregidor, (3) the events of our three years as prisoners and the story of medical work done there, (4) the liberation of the prison. Interspersed are the 'Bars,' or poems. Some of them are in a serious vein, while others are for the most part, of a humorous nature."

Doctor Brown was born in Tennessee and has lived most of his life in Texas. At present, as Major Brown, he is surgeon for the Army Medical School, recently moved to San Antonio from Carlisle Barracks, Pennsylvania. He is married and has a young daughter who thinks he writes "funny things." Doctor Brown adds a postscript in his letter to us: "I must tell you this: while I was a prisoner I was allowed to send a postcard to my wife after the first two years. Inasmuch as Francis Ticknor's little poem had always been a favorite of ours since childhood, I signed the card 'Little Giffen'—it told her more about my situation than a dozen pages, as you can well appreciate!"

M. L. Mc D.



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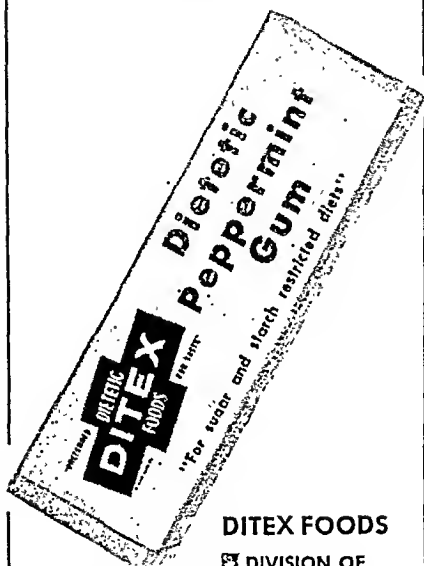
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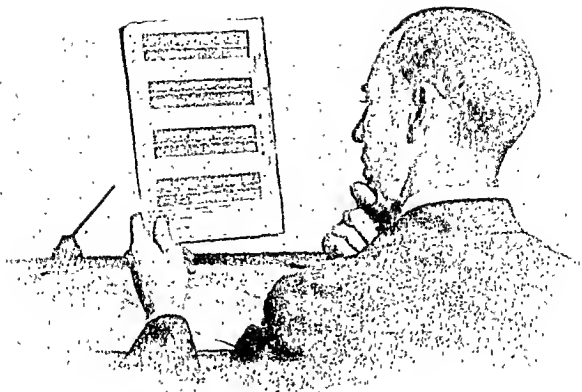
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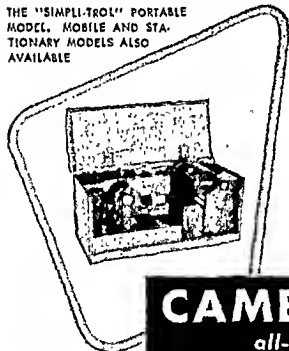


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* M. H. Barker Journal A.M.A. 106 (March 7, 1936) 762



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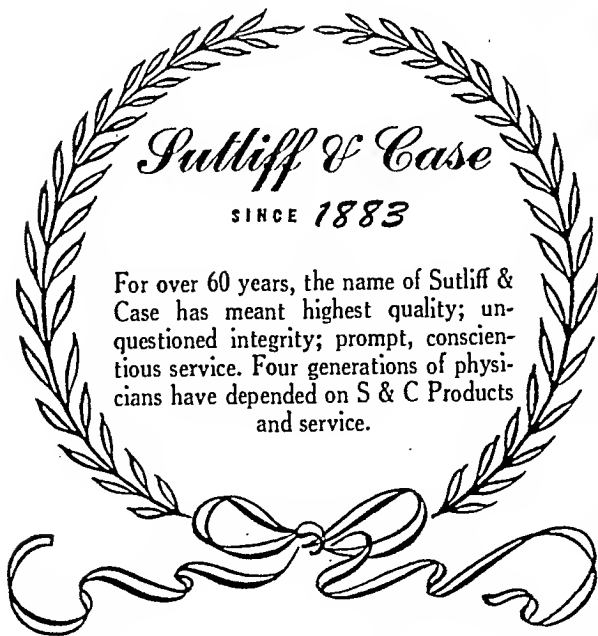
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VOLUME 1, Number 4

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Nelson W. Barker, M.D., CONSULTANT IN MEDICINE, UNIVERSITY OF MINNESOTA GRADUATE SCHOOL OF MEDICINE, ROCHESTER, MINNESOTA

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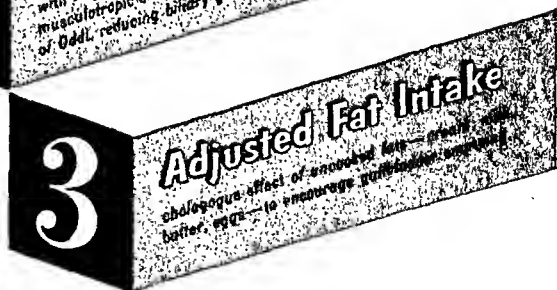
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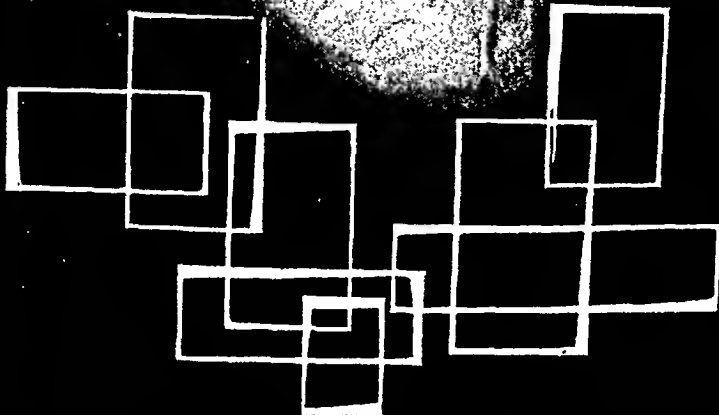
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OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA

APRIL, 1947

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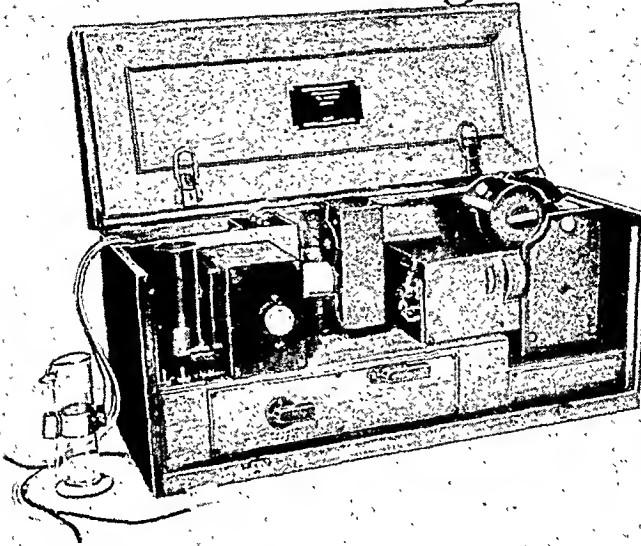
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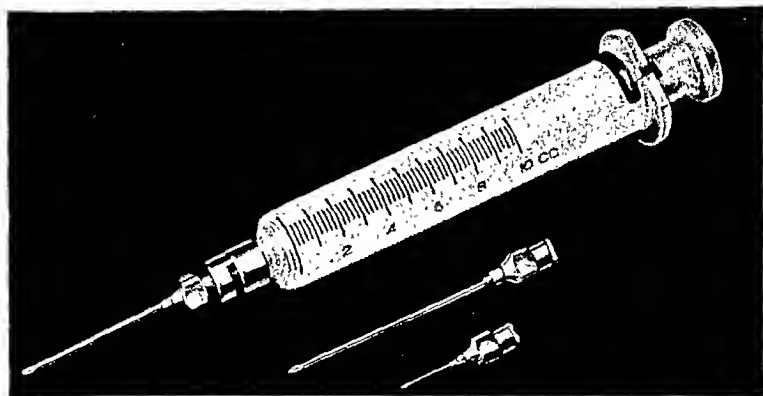
A 28-page paper, "A New Sensitive Portable Plethysmograph," by G. E. Burch, M. D. (Am. Heart J. 33: 48, January 1947), describes this instrument in detail. We shall be pleased to send one or more reprints of Dr. Burch's paper on request.



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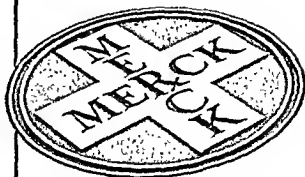
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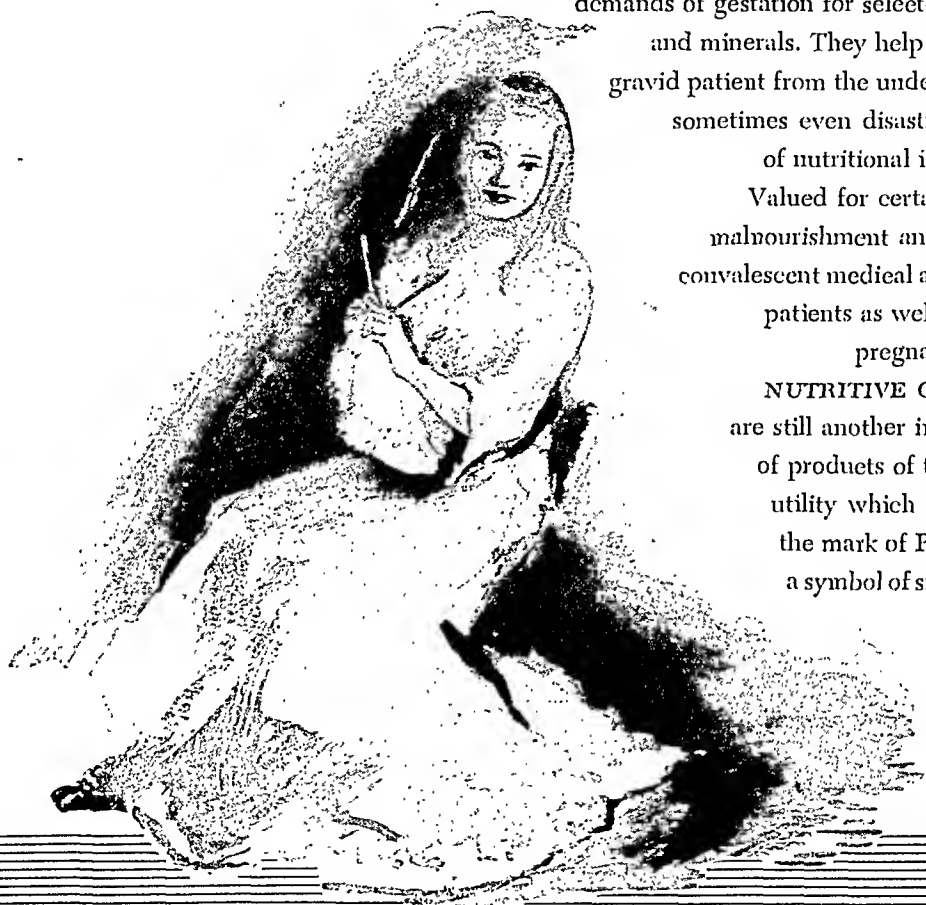


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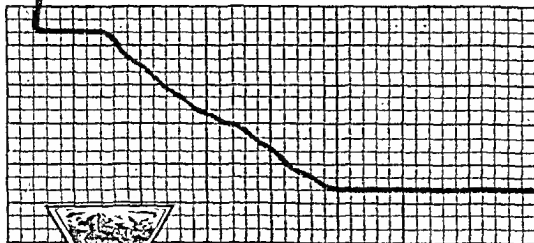
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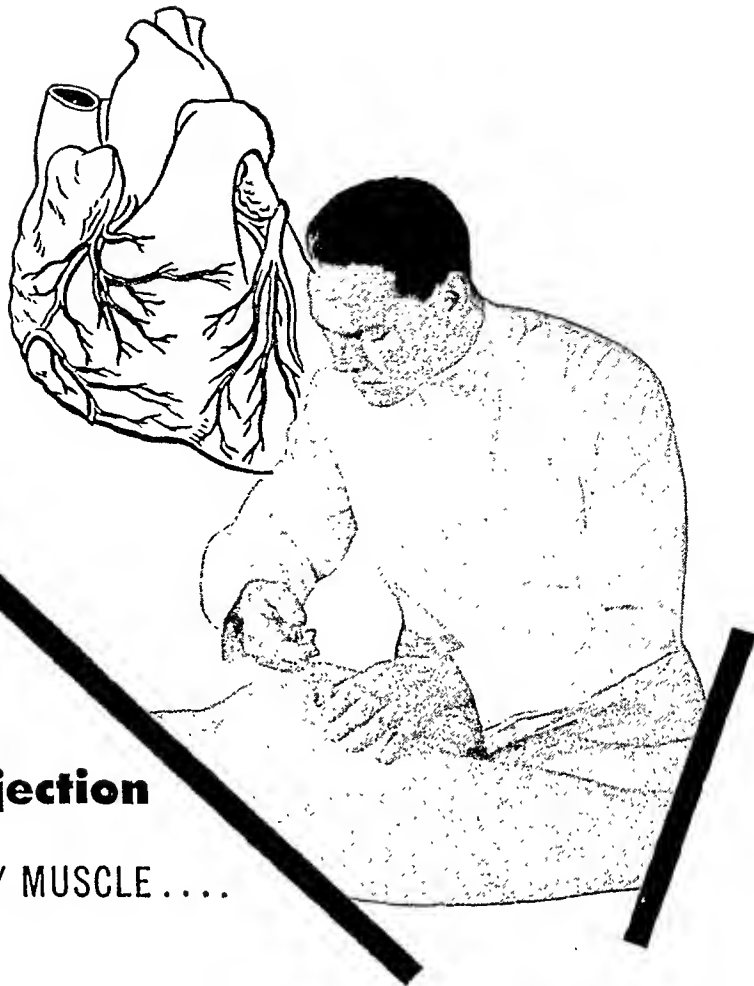
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2. Finkelstein, M. B. and Smyth, C. J.: Proc. Central Soc. Clin. Research, 16:69, 1943.
3. Friedgood, H. B.: New Eng. J. Med., 227:788-798 (Nov. 19) 1942.
4. Finkelstein, M. B. and Smyth, C. J.: J. Lab. and Clin. Med., 31:454, 1946.



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Anticoagulant Therapy in Thrombosis and Embolism

NELSON W. BARKER*

UNIVERSITY OF MINNESOTA GRADUATE SCHOOL OF MEDICINE, ROCHESTER, MINN.

THE seriousness of intravascular thrombosis and embolism and their potentiality to cause death or temporary or permanent disability have been well known by the medical profession since the days of Virchow and Welch; yet little progress has been made in understanding the mechanism of these pathologic processes in the last fifty years. It is generally recognized that intravascular thrombosis develops as a result of a lesion of the intima of a blood vessel, a slowing of the blood flow in a blood vessel, or an alteration in the coagulability of the blood, and that it usually results from a combination of two or all of these factors. Medical science has made almost no progress in efforts to inhibit thrombosis by prevention or treatment of lesions of the vascular endothelium. Efforts to prevent or eliminate slowing of the blood flow have been disappointingly ineffective. In recent years, however, two drugs, heparin and dicumarol, have been introduced which impair the coagulability of blood. Sufficient evidence has now accumulated to permit the statement that, when properly used, these drugs will prevent, or at least markedly inhibit, intravascular thrombosis by their

effect on the coagulability of blood regardless of the exact mechanism of the development of the thrombus. Neither drug is known to have any effect on a thrombus or embolus that already exists when administration of the drug is begun.

It would seem logical to assume that in order to prevent thrombosis under all conditions it would be necessary to render the blood totally incoagulable for prolonged periods, but obviously this involves considerable risk, since any interruption in vascular continuity would result in uncontrollable hemorrhage. The aim of anticoagulant therapy is to impair coagulability of the blood only partially; that is, to impair it sufficiently to inhibit thrombosis but insufficiently to allow uncontrollable bleeding. In spite of considerable variability of response to dicumarol and heparin among different patients and the relatively narrow zone of therapeutic effectiveness and safety, a satisfactory anticoagulant effect usually can be maintained if the patient is under daily medical supervision and if the blood is tested frequently. A few situations may be encountered in which the stimulus to thrombosis is so strong that it cannot be corrected by safe anticoagulant therapy, and likewise a few will be encountered in which bleeding will occur in spite of careful anticoagulant therapy.

*Consultant in Medicine, Mayo Clinic; Associate Professor of Medicine, University of Minnesota Graduate School of Medicine.

NOTE: Presented before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio, October 15 to 18, 1946.

HEPARIN

HEPARIN was first isolated from the liver of the dog by McLean¹ working in Howell's laboratory in 1916. However, its toxic effects precluded administration to human beings until a purified substance was obtained as a result of the investigations of Charles and Scott.² Purified heparin is now prepared commercially from beef lung and is dispensed in ampules containing 100 mg. of the drug in 10 cc. of solution. Milligrams have replaced the old units in computing dosage. When introduced into the blood stream in vivo or when mixed with blood in vitro, heparin has a strong anticoagulant effect although the exact nature of its action is uncertain. Chargaff and his co-workers³ have stated that it combines with a heparin complement in the blood, and that one or more such combinations inhibit the conversion of prothrombin to thrombin and the coagulation of fibrinogen by thrombin. The present commercial heparins are nontoxic and appear to have no other physiologic action than their effect on blood coagulability.

The laboratory test of anticoagulant effect of heparin in vivo is the simple test of coagulation time of venous blood withdrawn and placed in a glass tube. The degree of prolongation of clotting time following a single dose of heparin administered intravenously varies among different individuals, and it follows that varying amounts of heparin will be required to maintain a certain prolongation of clotting time among different individuals. This variation has been demonstrated by de Takats⁴ who devised a heparin tolerance test. It is noteworthy that patients who have certain thrombosing diseases are frequently more than normally resistant to heparin. As an anticoagulant, heparin has advantages in that it produces its effect rapidly (within five to ten minutes after a single intravenous injection) and that its effect can be terminated relatively rapidly (within a few hours) by discontinuing administration. Heparin has the disadvantages of being expensive and requiring time-consuming



NELSON W. BARKER

parenteral administration which is impractical for periods much longer than two weeks.

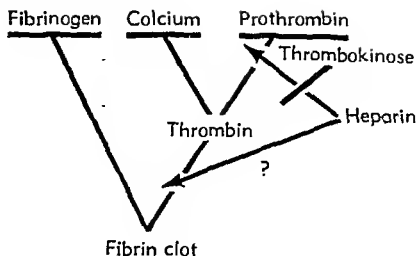
There are two methods for the intravenous administration of heparin. The first, or Toronto method,⁵ is by the continuous intravenous drip technic whereby 100 or 200 mg. (preferably the latter)⁶ of heparin is added to 1,000 cc. of diluent (either 0.9 per cent solution of sodium chloride or 5 per cent solution of glucose), and the administration of the dilute solution is begun at the rate of 25 drops per minute. Then the number of drops per minute is varied by adjusting the clamp on the tube so that the coagulation time of venous blood is maintained between fifteen and twenty-five minutes. It is necessary to determine the coagulation time every three to six hours at first and every twelve hours thereafter in order to be sure that the proper effect is maintained. Variations in sensitivity to heparin may occur in the same patient from time to time. It is also necessary to count the drops delivered each minute frequently in order to be sure that the desired

amount is being delivered. If the wrist is immobilized by a small splint, if a vein on the back of the forearm is used, and if there is plenty of slack tubing, the patient can move his arm around rather freely without dislodging a needle anchored only with adhesive tape. If rapid anticoagulant effect is desired at the onset of treatment, a single intravenous injection of 25 mg. of concentrated heparin may be given just before the continuous intravenous administration is begun.

The second, or Swedish method,⁷ of intravenous administration of heparin is to give frequent injections of a fixed amount of the concentrated stock solution. In Sweden a commonly employed dosage is 100 mg. every six hours. At the Mayo Clinic we have used 50 mg. every four hours. When this method is employed, the differences in sensitivity to heparin are disregarded as is the fact that the coagulation time has returned to normal for at least an hour before each subsequent injection. However, this method seems to be effective in preventing thrombosis. It is obviously simpler for short periods, such as a few days, but less desirable for long periods, such as two weeks, because of the frequent venipunctures.

Recently the deep subcutaneous administration of heparin in a slowly absorbed medium has been recommended by Loewe and his associates.⁸ Although less heparin per day is used and the effect of one injection is prolonged (usually for two days), there may be considerable pain and sometimes bleeding into the tissues at the site of injection. The rate of absorption may be accelerated by the local use of heat and slowed by the local use of cold, but the anticoagulant effect is not easily regulated or stopped. This method of administration, therefore, nullifies one of the advantages of heparin as an anticoagulant.

Several reports have indicated that heparinization prevents thrombosis in human beings. Murray and Best⁹ used heparin as a prophylactic measure after operations on 444 patients without encountering pulmonary embolism. Murray,¹⁰ McClure and Lam,¹¹ Crafoord and Jorpes,¹² and Bauer¹³ all have reported series of



Courtesy, Surgery, Gynecology and Obstetrics.

The theory of clotting (Howell). The three fundamental factors, fibrinogen, calcium and prothrombin are underlined. In the case of injury to tissues or after disintegration of platelets, thrombokinase (cephalin) is released and counteracts heparin so that prothrombin is free to join with calcium to form thrombin, which in turn unites with fibrinogen to form fibrin. (From "Heparin Tolerance—A Test of the Clotting Mechanism," by Geza de Takats, M.D., Chicago).

patients treated with heparin following non-fatal postoperative pulmonary embolism and thrombophlebitis without the development of further thrombo-embolic episodes. Murray¹⁰ has described the usefulness of heparin in preventing thrombosis following operations on the vascular system.

DICUMAROL

DICUMAROL [3,3'-methylene-bis-(4-hydroxy-coumarin)] was first isolated from spoiled sweet clover and was later synthesized by Link and his associates^{13, 14} at the University of Wisconsin. When administered to man and animals, dicumarol produces prothrombin deficiency as indicated by prolongation of the Quick prothrombin time. The mechanism by which the prothrombin deficiency is produced is still obscure, but it is likely that dicumarol or some derivative thereof depresses the formation of prothrombin in the liver. Curiously dicumarol has no other observable or measurable effect on the morphology or function of

the liver nor on any other organs of the body. Other than its effect on the prothrombin, dicumarol produces no toxic effects except rare minor allergic disturbances, such as urticaria and headache. Because of the prothrombin deficiency, coagulability of the blood is impaired by dicumarol but increase of coagulation time of whole blood in glass tubes does not parallel increase of prothrombin time and cannot be used as an index of the degree of effect. Clot retraction time usually is prolonged and the sedimentation rate of the erythrocytes usually is accelerated by dicumarol.¹⁵ There is also some evidence that the adhesiveness of platelets is reduced.^{16,17} Other than these no effects have been noted on the blood following administration of dicumarol.

As an anticoagulant dicumarol has the advantage of cheapness and effectiveness when administered orally (a satisfactory preparation for parenteral administration has not been developed). It has the disadvantages, first, that the effect is delayed for one or two days and sometimes longer after administration is begun and, second, that the effect persists for several days after administration is discontinued.¹⁵

Patients vary considerably in their sensitivity to dicumarol. Dietary deficiency, hepatic insufficiency, and renal insufficiency may greatly increase sensitivity. Decreased sensitivity has been noted among certain patients with thrombosing diseases. In general the degree of sensitivity cannot be predicted in advance. For these reasons and as a guide to the frequency of administration of doses of dicumarol, it is necessary that a Quick test of prothrombin time be done daily during the period of administration of the drug in order to be certain that an adequate but not excessive effect is being produced. The reports of prothrombin time must be consistently comparable from day to day. To this end it is necessary to use a thromboplastin of consistent potency in the tests. Since thromboplastins used in different clinics and hospitals may be of variable potency, and since thromboplastins prepared by the same technic also may vary, it is advisable that the

potency of any thromboplastin used in determination of prothrombin time, as a guide to dosage of dicumarol, be established frequently.¹⁸

Because of the variability in thromboplastins and the need for comparable figures, reports of prothrombin time preferably are expressed as percentage of normal prothrombin. These values, calculated in seconds and converted into percentages, can be determined for any thromboplastin by ascertaining the prothrombin time for undiluted normal plasma and for normal plasma diluted to various concentrations with 0.9 per cent solution of sodium chloride. The important prothrombin times to know for any thromboplastin are those for 100 per cent normal plasma and for 30 per cent, 20 per cent, and 10 per cent dilutions of normal plasma. In giving dicumarol the attempt is made to keep the concentration of prothrombin between 10 per cent and 30 per cent of normal because thrombosis will almost certainly be prevented if it is less than 30 per cent and bleeding is unlikely to occur if it is more than 10 per cent.

THE SCHEDULE of dosage for dicumarol which has been used successfully at the Mayo Clinic for five years is as follows.¹⁹ The entire amount for one day is given in a single dose. The first dose is 300 mg. Thereafter 200 mg. are given on each day that the value for prothrombin is greater than 20 per cent of normal prothrombin. On days that the value for prothrombin is less than 20 per cent of normal no dicumarol is given. If the value for prothrombin falls to less than 10 per cent of normal and remains there for more than one day, indicating more than usual sensitivity to dicumarol, 20 to 30 mg. of menadione bisulfite (synthetic vitamin K) is given intravenously, and thereafter only 100 mg. of dicumarol is given to that particular patient on days when the value for prothrombin is greater than 20 per cent of normal. If a patient is found to be very resistant to dicumarol, the dosage may be raised to 300 mg. on those days when the value

for prothrombin is more than 20 per cent of normal. Continuous prothrombin deficiency of between 10 per cent and 30 per cent of normal has been maintained in patients for as long as four to six months by administration of dicumarol without evidence of harmful effect and with return of prothrombin to normal levels within a few days after administration was finally discontinued.

TABLE 1

NONFATAL POSTOPERATIVE PULMONARY EMBOLISM AND INFARCTION

CASES	CONTROL GROUP; ANTICOAGULANTS NOT ADMINISTERED		DICUMAROL ADMINISTERED AFTER EPISODE	
	Number	Per Cent	Number	Per Cent
Total cases	678	100	292	100
Subsequent venous thrombosis, pulmonary embolism or infarction . .	297	43.8	3	1.0
Subsequent fatal pulmonary embolism	124	18.3	1*	0.3

*After the value of prothrombin had returned to normal.

TABLE 2

POSTOPERATIVE THROMBOEMBOLISM

CASES	CONTROL GROUP; ANTICOAGULANTS NOT ADMINISTERED		DICUMAROL ADMINISTERED AFTER DIAGNOSIS	
	Number	Per Cent	Number	Per Cent
Total cases	897	100	280	100
Subsequent venous thrombosis, pulmonary embolism or infarction . .	327	36.3	8*	2.8
Subsequent fatal pulmonary embolism	51	5.7	0	0

*One case of minor pulmonary infarction and seven cases of thrombophlebitis, in three of which the value for prothrombin was greater than 30 per cent of normal when the recurrence developed.

The most efficient anticoagulant therapy is obtained with doses of dicumarol and preliminary heparinization. In such a program administration of heparin and dicumarol are begun simultaneously, dicumarol by the usual schedule of dosage, and heparin at the rate of 50 mg. of the concentrated solution intravenously every four hours. Administration of heparin is discontinued when the concentration of prothrombin has fallen to less than 20 per cent of normal. This usually occurs within thirty-six to seventy-two hours after administration of the first dose of dicumarol. Blood

for the daily tests of prothrombin time should be withdrawn four hours after an injection of heparin has been given.²⁰ This program gives a prompt anticoagulant effect and is easily and cheaply maintained for prolonged periods if desired.

The effectiveness of dicumarol as an anticoagulant has been demonstrated in animals by several experiments.^{21, 22, 23} Its effectiveness in the human being has been demonstrated both by comparative statistics of series of patients who have had postoperative thrombophlebitis and pulmonary embolism and have been treated with or without dicumarol²⁴ (Tables 1 and 2) and recently by comparative statistics of the incidence of arterial and venous thrombosis and embolism among patients who have had acute coronary occlusion and have been treated with or without dicumarol.

RISK OF BLEEDING

THE ONLY hazard of anticoagulant therapy is risk of bleeding. Although some writers have tended to exaggerate this risk, the chances of bleeding are small if the plans of dosage of the drugs are followed carefully, if the patient is under continuous medical supervision, and if the contraindications to anticoagulant therapy are observed. The risk is somewhat less with heparin than with dicumarol because the anticoagulant effect of heparin can be stopped more quickly than the anticoagulant effect of dicumarol if bleeding occurs. Widespread hemorrhages or ecchymoses are almost unknown as the result of therapeutic doses of dicumarol. Minor bleeding, such as transient epistaxis, microscopic hematuria, or isolated ecchymosis, occurs in about 3 per cent of cases and can be disregarded. Major bleeding during administration of dicumarol consists of slow but usually persistent oozing from operative wounds, around drainage tubes, or from ulcerative lesions of the gastro-intestinal tract. It has been noted in only 1 per cent of patients who have had thrombosis or embolism at the Mayo Clinic and in 2.5 per cent of those who have not had thrombosis or embolism but have

been treated prophylactically for these complications.²⁴ In more than 2,000 cases in which treatment with dicumarol has been used, we have observed five cases of fatal hemorrhage. All but one of these five cases occurred early in our experience with the drug and before we appreciated some of the contraindications. In three of the five cases the patients were in advanced stages of diseases with hopeless prognoses.

When major bleeding occurs during administration of dicumarol, 500 cc. of freshly drawn citrated blood should be transfused to the patient. This restores lost blood and to some extent provides a temporary supply of extra prothrombin. Transfusions should be repeated once or twice daily until bleeding ceases. Also, the patient should be given 60 mg. of menadione bisulfite intravenously. In most cases the prothrombin time will gradually fall to near-normal limits within twenty-four hours after such an injection¹⁸ but if it does not, the injection can be repeated daily until bleeding ceases.

CONTRAINDICATIONS

IN MY experience the following conditions contraindicate anticoagulant therapy. (1) Subacute bacterial endocarditis, purpura of any type, and blood dyscrasia with tendency to bleed contraindicate use of anticoagulants because of the greatly increased bleeding tendency in these patients. (2) Hepatic or renal insufficiency contraindicates the use of dicumarol because severe and prolonged prothrombin deficiency may develop after small doses of this drug in such cases. Use of heparin is not contraindicated. (3) Recent operations on the brain or spinal cord contraindicate use of anticoagulants, not because of the increased bleeding tendency, but because of the serious consequences of even a small amount of bleeding at the operative site. (4) The existence of ulcerative lesions, open wounds, drainage tubes in operative wounds, the renal pelvis, or the common bile duct, or the presence of indwelling catheters or duodenal drainage tubes in-

serted through the mouth or nose all increase the risk of bleeding around the tube or from granulation tissue. Such cases call for extra caution if anticoagulants are used, but the risk is not prohibitive. If thrombosis has occurred in such a case, the risk of bleeding may be much less than the risk of further thrombosis and embolism. (5) If surgical operation is found necessary in a case in which anticoagulant therapy with dicumarol is being administered, the prothrombin time should be brought to normal before the operation is done and the anticoagulant treatment may be resumed after the operation.

USES OF ANTICOAGULANT THERAPY

Postoperative thrombosis and embolism—The rationale for the use of anticoagulants for patients who have had postoperative pulmonary embolism and survived is the great risk of further thrombosis (44 per cent of cases) and of fatal embolism (18 per cent).²⁵ In many cases the source of the first embolus is unknown since there is no clinical evidence of venous thrombosis or thrombophlebitis, but the patient is marked as having a tendency to thrombosis. Table 1 illustrates the effectiveness of anticoagulant therapy in cases of postoperative pulmonary embolism.

The patient who has clinical signs of venous thrombosis or thrombophlebitis also is marked as having a tendency to thrombosis. If no treatment is given, recurrent or extending thrombosis is likely to occur in 25 per cent of the cases and fatal embolism in 6 per cent.

There is clinical and pathologic evidence to favor the concept that pulmonary embolism only develops when a thrombus is fresh—that is, minutes to a few hours old, and almost never after it is three days old. Thus by the time venous thrombosis is recognized clinically, the danger of detachment of that thrombus almost certainly is over. Embolism only occurs if there is fresh propagation of the thrombus proximally or if a new thrombus develops in a distant vein. Anticoagulant therapy is given to patients who are known to have postoperative venous thrombosis or throm-

bophlebitis to prevent proximal extension of the thrombus or fresh thrombosis elsewhere. When anticoagulant treatment is properly given, extension of thrombosis and pulmonary embolism almost never occur (Table 2). This gives further support to the concept that an embolus only comes from a fresh thrombus.

Patients who give histories of having had thrombophlebitis or pulmonary embolism under any circumstances and at any time prior to a surgical operation are known to have a greatly increased risk of postoperative thrombophlebitis and pulmonary embolism. Anticoagulant therapy, as a prophylactic procedure, is rational and advisable in these groups of cases. It might seem logical to give prophylactic anticoagulant therapy to all surgical patients in the immediate postoperative period. At present, however, this is impracticable and hardly justifiable. Venous thrombosis afflicts only about 1 per cent and fatal embolism only about 0.2 per cent of unselected patients who have undergone operation.²⁰ Special supervision and at least one daily blood test are necessary when anticoagulant therapy is being used, and the risk of bleeding is somewhat higher in those cases in which thrombosis has never occurred than in those in which it has. However, an increased risk of postoperative thrombosis follows laparotomy in the presence of obesity, varicose veins, heart disease, anemia, infection, or a malignant neoplasm, and prophylactic anticoagulant therapy may be justified in such cases.

For patients who have had postoperative thrombosis or embolism, anticoagulant therapy with dicumarol should be given as soon as the diagnosis is made. Preliminary heparinization is advisable for those who have severe pulmonary embolism but is apparently unnecessary otherwise. When given as a prophylactic measure only, administration of dicumarol should be started on the third postoperative day. In all cases the prothrombin deficiency should be maintained for at least ten days, until the patient has been ambulatory at least three days, or until the patient is ready to leave the hospital.

Posttraumatic thrombosis and embolism—Although statistical evaluation is lacking, the results of anticoagulant therapy seem to be equally good in cases of venous thrombosis and pulmonary embolism that follow fracture and other severe injuries. The same principles apply here as in postoperative thrombosis and embolism, plus the additional factor that the period of rest in bed may be considerably longer. Therefore anticoagulant therapy must be continued for longer periods.

Postinfectious thrombosis and embolism—It has long been known that thrombophlebitis and pulmonary embolism may complicate many infectious diseases, such as typhoid fever and pneumonia. Anticoagulant therapy has been found effective in preventing further thrombophlebitis and embolism during convalescence in a small series of such cases.

In chronic ulcerative colitis complicated by thrombosis and embolism, the decision on whether or not to use anticoagulant therapy may be difficult because of the risk of increased bleeding from the colon and the fact that the disease is chronic. At the clinic, however, we have used it in a number of such cases for prolonged periods without untoward result.

Postpartum thrombosis and embolism—At first dicumarol was thought to be contraindicated during the postpartum period because of danger of uterine bleeding. However, experience in a small series of cases has shown that no uterine bleeding occurs during treatment with dicumarol if the uterus is involuting normally and if administration of the drug is not started until the sixth postpartum day. Evidence of further thrombosis or embolism has not been observed when dicumarol has been given, but the series of cases observed has been too small to permit statistical evaluation. In one carefully studied case no anticoagulant effect was transmitted to the infant through the breast milk of a mother who was receiving dicumarol.

Congestive heart failure with venous thrombosis and pulmonary embolism—Dicumarol has been given in a small series of cases of con-

gestive heart failure in which venous thrombosis and pulmonary embolism developed. Thrombo-embolic complications did not recur during the period of anticoagulant therapy. The temporary use of dicumarol is predicated on the premise that ultimately compensation can be restored in these cases and that then the danger of thrombosis will cease. Administration of dicumarol should be continued until the patient is ambulatory.

Recurrent idiopathic thrombophlebitis—Anticoagulant therapy is impractical in most cases of recurrent idiopathic thrombophlebitis because episodes may recur for years and the interval between episodes may be long. However, in a few cases in which frequent repeated episodes interspersed with episodes of pulmonary infarction occur, dicumarol may be of value to stop the disease temporarily and may succeed in producing a remission which will persist for some time after administration is discontinued.

Acute coronary occlusion with myocardial infarction—The incidence of thrombotic complications, namely, cerebral and peripheral arterial thrombosis or embolism, venous thrombosis, and pulmonary embolism, has been shown to be high after acute coronary occlusion particularly in the first six weeks (35 per cent of cases according to Nay and Barnes.)²⁷ Recently three excellent reports have appeared on series of cases in which acute coronary occlusion has been treated with and without dicumarol.^{28, 29, 30} A marked reduction in incidence of thrombo-embolic complications was noted among those patients treated with dicumarol. There is some, but not conclusive, evidence that the risk of a second coronary occlusion is lessened as well. When dicumarol is used in acute coronary occlusion, administration should be begun as soon as possible after the occlusion has occurred and should be continued for four to six weeks. Preliminary heparinization is advisable in severe cases.

Acute arterial occlusion of the extremities—In arterial embolism of the extremities there is danger of thrombosis propagating distally

from the embolus which will produce gangrene after the arterial spasm relaxes. There is also danger of further intracardiac thrombosis and therefore recurrent embolic episodes.

In acute arterial thrombosis in situ in the extremities there is danger of progressive thrombosis which increases the possibility of gangrene. Therefore anticoagulant therapy is indicated in acute arterial occlusion of the extremities regardless of the cause of the occlusion.³¹ Dicumarol should be given as soon as possible after the occlusion develops, and preliminary heparinization should be used.

Cerebral arterial thrombosis—Anticoagulant therapy has rarely been used in treatment of cerebral arterial thrombosis. In some cases cerebral hemorrhage cannot be entirely excluded in the differential diagnosis. There is the theoretical risk of producing hemorrhage at the site of infarction in the brain and thereby increasing the damage. Rarely, there may be almost certain clinical evidence of progressive cerebral arterial thrombosis, and in such a case the use of heparin or dicumarol with preliminary heparinization may be considered.

SUMMARY

Anticoagulant therapy with heparin or dicumarol is effective in the prevention of intravascular thrombosis. It requires careful daily supervision and individualization of dosage of the drug which is used. There is a small risk of serious bleeding. Dicumarol should be used only if facilities are available for accurate and comparable determinations of the prothrombin time. There are certain contraindications to the use of both heparin and dicumarol. Adequate experience has demonstrated the value of anticoagulant therapy particularly with dicumarol in postoperative thrombosis and embolism, acute coronary occlusion, and acute arterial occlusion of the extremities. It appears to be equally effective in thrombosis and embolism complicating severe injuries, the puerperium, congestive heart failure, and infectious diseases, although experience in these cases has been insufficient for definite conclusions to be drawn.

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Pitfalls in Spinal X-Ray Diagnosis

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ANY discussion of radiological diagnosis of spinal conditions must of necessity be prefaced by a few words concerning technic. Owing to the complex anatomy of the spine it is evident that technically excellent films are necessary before a considered opinion can be given. Many variations of the conventional positions also are essential when particular portions of the spine are in question.

Another pertinent general statement is in order before considering individual lesions and their simulants—the examiner, not only in radiology, but in all other branches of clinical medicine, should adopt the slogan, “What might it be, besides what I think it is?” If this is kept in mind—and applied—far fewer mistakes will occur, and only in this way will some of the more unusual conditions be properly pigeonholed. Do not jump to a hasty conclusion because on superficial examination the appearance resembles something seen previously. Examine all films critically and base your conclusion on such a study. Do not form an opinion hastily, trying to make the criteria fit into a preconceived snap diagnosis.

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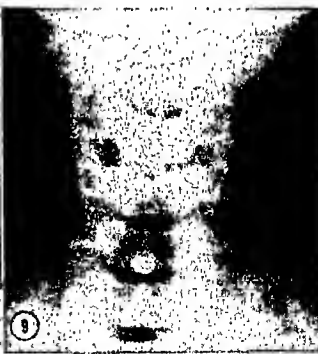
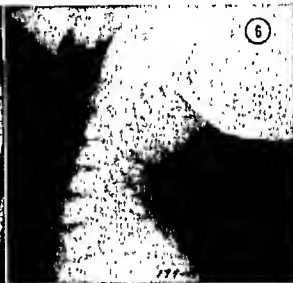
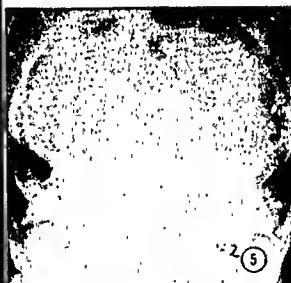
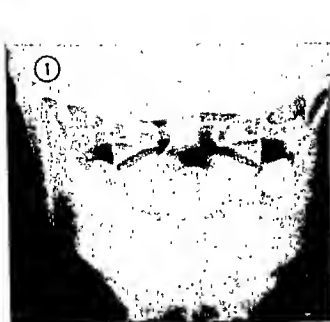
NOTE: Read before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio, October 15 to 18, 1946.

One should have a definite routine for examining bone films, such as first studying the contour of the bones, secondly, the bone texture, thirdly, the relationship of bone to bone at the articulations, and, finally, examination of the soft tissues. Above all, a final opinion should not be based on examination of wet films.

CERVICAL SPINE

We feel that examination of the cervical spine is incomplete without at least two oblique views, rotating the neck 45° to each side, in addition to the conventional anteroposterior and lateral views. At these angles, one is looking directly through the intervertebral foramina and can thus see any encroachment on the lumina of these important, small, circumscribed bony channels. Partial dislocation may throw an articular facet into the canal, or an hypertrophic rim of new bone may partially block the small openings, thus giving rise to pressure on one or more divisions of the brachial plexus. This is important in pain or numbness radiating down the arms, or in occipital headaches.

In suspected lesions of the first and second cervical vertebrae, the odontoid process—the tongue-like projection of the second inside the first—also should be visualized. This can be



accomplished by propping the jaws open with a cork, and accurately centering the angle of the x-ray so as to miss the base of the skull and the mandible (Fig. 1). Another method is to have the mandible in constant motion while the film is being made, thus blurring out the mandible. In this manner, fractures of the odontoid at its base and compression fractures of the first vertebra may be demonstrated. Occasionally there is a congenital absence of the odontoid, leading to instability of this joint (Fig. 2).

Fractures of the base of the odontoid can be visualized on good films made in this fashion. Usually there is also a displacement forward of the body of the first on the second vertebra (Fig. 3), and if this is seen, it is well to try and visualize the fracture through the open mouth.

FRACTURES of the posterior ring of the first cervical are visualized more readily in the oblique position (Fig. 4). There is, however, a not infrequent failure of fusion of the posterior process, which might be mistaken for fracture. This is more often seen in films of the posterior portion of the skull, through the foramen magnum (Fig. 5). The ends are smooth, however, not sharp and jagged as in fracture. Fractures of the pedicles of the cervical vertebrae usually are demonstrated only in the oblique views.

Fractures of the spinous processes are usually obvious, if the films are carefully studied. Occasionally sesamoids develop in the soft tissues, but these are smooth and widely separated.

Self-reducing dislocations of the cervical spine occur. When the usual films do not demonstrate injury, and clinically it is there, it is well to take lateral films with the neck in extension and flexion (Figs. 6 and 7). The calcified cartilages of the larynx should not be mistaken for anomalies.

Congenital fusion of the bodies, the so-called Klippel-Feil syndrome, may be confused with fusion due to infection. There is, however, no



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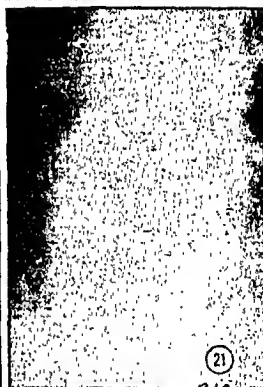
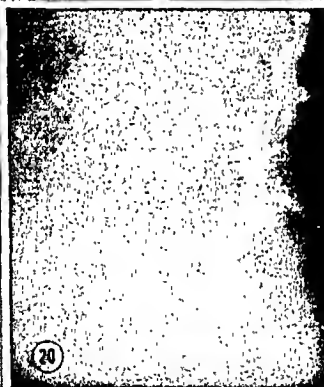
ring of reactive bone, as is seen in infection, and there is fusion of the articular facets and pedicles. This anomaly may involve any two or three of the cervical bodies (Fig. 8).

Air in the slit of the larynx may simulate spina bifida, but one may follow this down into the enlarging trachea, thus eliminating the possible error in interpretation (Fig. 9).

DORSAL SPINE

The conventional anteroposterior and lateral views usually are sufficient in the dorsal spine, with the exception of the upper three dorsal vertebrae. To obtain a lateral view, it is necessary either to rotate the body slightly, or to take a lateral with one arm over the head to throw the shoulder girdle out of the way.

Confusing appearances are centers of ossification, which by location may readily be eliminated as chip fractures. Transverse vascular markings may persist into adult life, and if this possibility is kept in mind, the thought of a transverse linear fracture, which rarely if ever occurs, can be eliminated.



The anterior process of the first cervical (Fig. 10) may persist as a separate ossicle, or the odontoid articulation may simulate fracture. If one simply realizes the extremely remote possibility of such a fracture, one will properly catalogue this as an abnormality of no clinical significance instead of a fracture.

Accessory centers of ossification of the transverse processes of the dorsal vertebrae, more frequently the first (Fig. 11), conceivably could be misinterpreted as fracture. The smoothness of outline, the location, and bilateral position should put the observer on his guard. Transverse processes of the dorsal spine may be fractured, but these are almost uniformly adjacent to the bodies, and the lines are sharply defined, not rounded.

Cervical ribs are very frequently seen, but should cause no difficulty in interpretation. The catch in this situation is correlating the finding of cervical ribs with symptomatology. In a great many instances cervical ribs cause no symptoms whatsoever, and the presence of cervical ribs may lead the unwary into considering them as the cause of symptoms, whereas an associated protrusion of a cervical intervertebral disc, or encroachment upon the cervical intervertebral foramina, is the real cause of the symptoms.

Erosion of the anterior margins of the bodies of the dorsal vertebrae is almost invariably due to aneurysm of the aorta, and with this finding it is up to the examiner to prove that it is not aneurysm.

LUMBAR SPINE

Examination of the lumbar spine, as in the cervical spine, consists in individualizing the procedure. If the low back is suspected, in addition to an anteroposterior and lateral covering the lumbar spine, a lateral should be made centering directly over the lumbosacral joint. Oblique views at 45° angles also are highly desirable in order to visualize the articular facets and their joints.

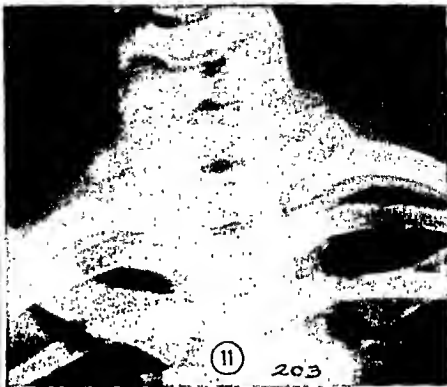
A FREQUENTLY overlooked back injury is a fracture of the articular facets (Fig. 12). A simulant is an accessory center of ossification, which, however, may be differentiated, since the line of cleavage of the accessory center is smooth and its lateral margins are slightly rounded, whereas in fracture, the line is usually jagged and sharply defined.

Rudimentary ribs arising from the twelfth dorsal may trick the unwary into a diagnosis of fracture of the transverse process. Here again, the junction lines are smooth or slightly rounded (Fig. 13). The shadow of the psoas muscle often simulates fracture of the transverse processes, but on good films it may be followed beyond the borders of the transverse processes.

As in the dorsal spine, centers of ossification for the bodies may simulate fracture and may persist into adult life (See Fig. 14, which is of a patient thirty-eight years old). The location and smooth contour should offer no difficulty in interpretation.

The lumbosacral region presents more developmental anomalies than any other portion of the bony skeleton; 20 to 25 per cent of all individuals show some variation from the conventional bony pattern, most of them entirely without symptoms. For this reason, anomalies in this region must be very closely correlated with a careful orthopedic or neurosurgical examination before they are regarded as being the cause of symptoms. In our clinic we have seen many patients with anomalies of the lumbosacral area entirely relieved of symptoms following removal of a protruding intervertebral disc. Spina bifida is very common, and should be disregarded unless it is very marked and is associated with neurological signs. Partial sacralization of the lower lumbar segment may, or more frequently may not, be the cause of symptoms (Fig. 15). Difference in the facing of the lumbosacral articular facets gives rise to a structural weakness which may result in a weak low back.

One anomaly sooner or later leads to low back symptoms, and that is a congenital cleft in the posterior process of the fifth lumbar,



eventually leading to anterior slipping of the body of the fifth on the sacrum (Fig. 16).

Infections of any portion of the spine are characterized almost invariably by involvement of the intervertebral disc with narrowing of the joint space and destruction in the adjacent bodies. This differentiates disease from malignancy in which there is destruction in the body but no joint narrowing. Before chemotherapy it was not so important to differentiate between the infecting organisms, since about all one could do was to diagnose a spinal infection, put the patient on a frame or in a cast, cross one's fingers, and have the patient pray. With the specificity of chemotherapy for some organisms, a bacteriological diagnosis is important. Tuberculosis, streptococcic and staphylococcic infections, as well as brucellosis will give almost identical pictures (Fig. 17, tuberculous, Fig. 18, streptococcus and staphylococcus, Fig. 19, brucellosis). Very rapid destruction is usually pyogenic. Spotted calcification with a soft tissue mass is almost uniformly due to spinal tuberculosis. A definite bacteriological diagnosis can be made in many instances by aspiration of the affected area.

COMPRESSION of any vertebra may be due to trauma, but the observer should always keep in mind that pathological fracture of a vertebra is frequently the presenting symptom in malignancy or in certain general constitutional disturbances. The bone texture should be examined most carefully in all such fractures (Fig. 20, metastatic malignancy). Multiple myeloma (Fig. 21) is a not infrequent offender, and blood studies, urinalysis, and usually sternal marrow puncture are definitely indicated, if radiological examination of the skull and ribs fails to show the characteristic punched-out areas. Hyperparathyroidism will give the same compressed decalcified appearance in the spine. Examination of the skull

may be helpful in this, since it may show the typical cystic appearance, sometimes with areas of increased density. Blood chemistry showing elevation of calcium and decrease of phosphorus is characteristic.

A simulant of destruction of a vertebral body is gas overlying the vertebra. This may be eliminated by following the shadows of decreased density beyond the vertebral body, or by making oblique views.

Paget's disease frequently involves the spine, and the appearance is quite characteristic. Longitudinal, wavy, heavy striae may be seen in the vertebral bodies.

Hemangioma of the vertebrae looks much like Paget's in that there are increased longitudinal striae, but these are not as thick or wavy as in Paget's. Blood chemistry also will help in diagnosis, since Paget's shows high serum alkaline phosphatase, with all other determinations being normal, whereas in hemangioma all the blood chemistry is normal.

Massive calcium deposition about one section of the spine, with disintegration of the bodies, is fairly characteristic of a Charcot spine (Fig. 22). The serology history is helpful when this is seen.

A massive density in the body of one vertebra may be a purely developmental abnormality, the so-called ivory vertebra, having no clinical significance, but the observer should think also of carcinoma metastasis from the prostate, which occasionally gives a very similar appearance (Fig. 23).

SUMMARY

The spine is a very complex structure, suffering all of the diseases of any other part of the skeletal system. In addition, it has others peculiar to it alone. Unless the radiological examiner has a thorough knowledge of normal spinal anatomy, technic, anomalies, and possible confusing appearances, an erroneous interpretation will be given.

Practical Points in the Diagnosis and Treatment of Actinomycosis and Sporotrichosis

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THE diagnosis of most fungous infections may be accomplished by one or a combination of several methods. These comprise clinical observations, which may be specific or pathognomonic in some cases or confusing in widespread or conglomerate lesions, histopathologic study of the biopsy material, mycologic demonstration of the causative agent (the best assurance of a correct diagnosis), and various laboratory procedures such as immunologic phenomena including serology, hypersensitivity, and other laboratory studies and clinical technics. These will be taken up in order for the diseases actinomycosis and sporotrichosis.

ACTINOMYCOSIS

Definition—Actinomycosis is a local or malignant disease which is granulomatous in nature and may be acute, subacute, or chronic. It is characterized chiefly by sinuses and fistulae, from which may be isolated variously colored granules which are masses of mycelium of species of the genera *Actinomyces* and *Nocardia*.

Clinical manifestations—Actinomycosis may be divided into two main groups, the cutaneous and the visceral. The cutaneous type may be

either primary, occurring in the epidermic layer as a nodule which extends into the corium and subcutaneous layers, or secondary to a deep-seated infection which usually occurs in the tissue closely associated with the buccal, thoracic, or abdominal cavities and pushes its way to the superficial layers of the skin.

In primary actinomycosis of the skin, the inoculation type, the fungus penetrates into the skin, and produces a nodule which pushes its way into the deeper layers of the cutis and then enlarges and extends to the superficial region of the skin. The nodule softens at the surface, becomes fluctuant, and finally ruptures, exuding a seropurulent or sanguineous material containing the so-called sulfur granules, the fungous structures characteristic of actinomycosis. The ruptured nodule becomes ulcerous and eventually scarred, or it forms a crust which does not allow the lesion to heal rapidly. Quite often new nodules form in the vicinity of the first nodule, and these then go through the same type of evolution. The lesions change in color from pink to dusky red. The formation of nodules in an area should suggest actinomycosis, but such a mass of ulcerated nodules may mimic a carcinoma, blastomycosis, syphilis, and at times, tuberculosis.

Cutaneous lesions secondary to subcutaneous involvement manifest themselves clinically as subcutaneous nodules or tumors that are rather firm in nature and livid in hue. These increase in size, soften, fluctuate, and

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break down, also giving off a seropurulent discharge containing the granules. As a result of the breaking-down of these lesions, fistulae are produced which become intercommunicating and through which the fungi are distributed, thus setting up new foci of infection. The surrounding skin then becomes a mass of granulomatous material with an oozing discharge. The picture becomes very confusing and simulates at times a carcinomatous overgrowth.

SKIN lesions secondary to subcutaneous involvement occurring in the head or neck region form the cervicofacial type. Actinomycosis in this region makes up approximately 57 per cent of the total number of cases. The diagnosis of the disease in this area is often relatively easy since the symptoms and signs are fairly characteristic. The fungus may be found as a normal inhabitant in the mouths of some individuals, usually without pathologic significance, particularly in and about carious teeth, folds of the gums, and tonsillar crypts. Following trauma such as is created by tooth extraction or tonsillectomy, the fungi are disturbed and set free, and are able to grow and produce disease.

In its visceral manifestations, actinomycosis usually shows a series of anatomical involvements beginning with the tongue and extending to the tonsils, pharynx, pulmonary system, gastro-intestinal tract, urinary tract, generative organs, cerebrospinal system, and osseous structures. The destructive process involved here is essentially similar to that seen in the cutaneous type with the formation of nodules that eventually rupture and produce more lesions. Multiple abscesses may be formed, and the infecting organism attacks adjacent tissue with the ultimate production of sinuses which reach the surface of the neighboring skin.

Chest or thoracic actinomycosis is primary in approximately 15 per cent of the cases. Infection of the lungs may result from an extension of the infectious process downward from the buccal or pharyngeal cavities, from the inhalation or ingestion of pathogenic actinomycetes from the air or dust, or on hay, straw,

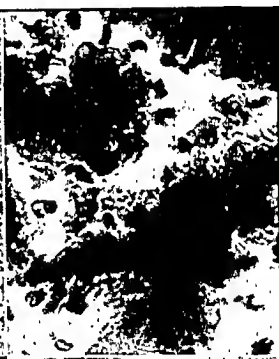
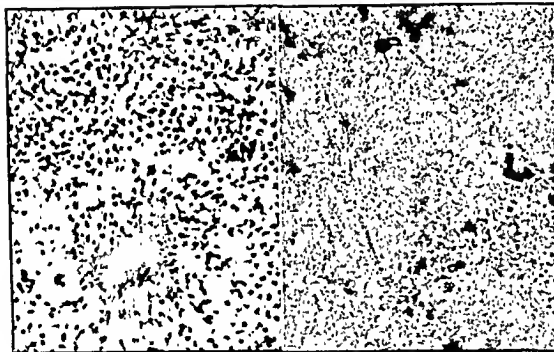
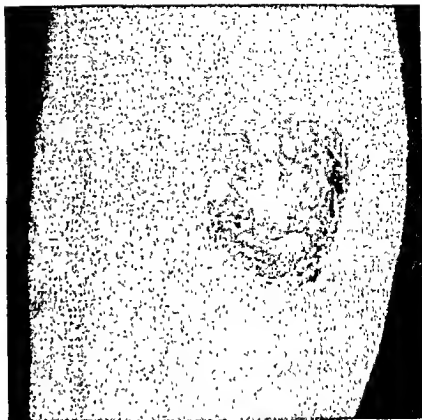
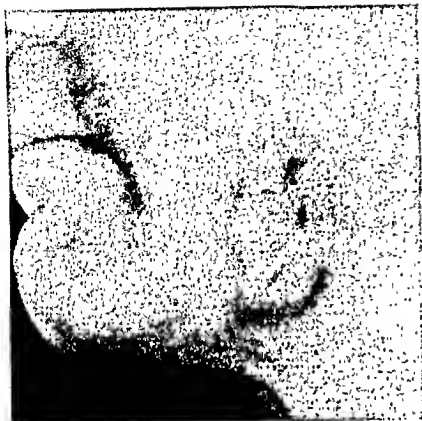


MORRIS MOORE

or other materials, or by the hematogenous spread of the fungi. Pulmonary involvement may also be secondary to intra-abdominal or pelvic actinomycosis. Lung lesions may be seen in progressive stages affecting the bronchi—the bronchitic type—the alveoli—the pneumonic type—and the lung lobes—the pleuropneumonic type. The abscesses that are formed enlarge, rupture, and empty the purulent material into the pleural cavity, and the patient experiences pleural pain. The pus may burrow its way to the skin, forming sinuses which are suggestive of a tuberculous process, and it may attack the pericardium, the vertebral column, and other organs.

There is a fourth or metastatic type which is characterized by the hematogenous spread of the fungi with resultant nodules. This stage may mimic metastatic pulmonary carcinoma or perhaps miliary tuberculosis. The possibility of tuberculosis should be carefully considered and may often be ruled out on the basis that the primary sites of actinomycosis are usually in the lung bases.

Roentgen examination of the lungs usually



(Upper left) Actinomycotic nodules of cheek secondary to gum involvement.

(Upper right) Primary actinomycosis of calf, inoculation type, resembling blastomycosis.

(Left, above) Actinomycotic nodule in lung tissue with young granule in center. Hematoxylin and eosin stain, X 245.

(Center, above) Soft granules in pus without clubs. KOH preparation, X 740.

(Right, above) Hard granules in lung tissue with radiate formation. Note glass-like appearance of granules. Hematoxylin and eosin stain, X 630.

(Lower right) Actinomycotic granule stained by the Gram Weigert method. The fungus is gram-positive and the radiate substance is acidophilic, X 1860.



reveals definite pneumonitis, fibrotic infiltration, and perhaps consolidation, either as massive areas or as small nodules seen as irregular areas of rarefaction. Pleural involvement with adhesions and general pleuritis with an accumulation of fluid, which may or may not be encapsulated, may be seen in advanced cases.

Abdominal actinomycosis makes up approximately 22 per cent of the reported cases. Lesions usually result from swallowing organisms present in the saliva, by the ingestion of contaminated foods, extension of the process from the thorax, and by the spread of lesions arising in the region of the ileocecal valve, the appendix, and the colon, where the organism may be a normal inhabitant. The resultant lesions may suggest clinically acute or subacute appendicitis, and the patient presents symptoms such as loss of weight, increasing weakness, spiked fever, night sweats, chills, and intestinal upset with vomiting. The infectious process produces sinus formation, granulation tissue, and connective tissue proliferation, ultimately resulting in "woody" induration, and the whole resembling carcinoma. Retroperitoneal spread of the infection results in urinary tract infection with symptoms simulating cystitis, pyelonephritis, hypernephroma, and carcinoma, and may also involve the lumbar vertebrae with resultant compression of the spinal cord or the formation of a psoas abscess. Osseous involvement is not an infrequent complication.

Diagnostic procedures—With the exception of the demonstration of the pathogens either in tissue or pus and the culturing of the causative fungi, laboratory procedures have not been very satisfactory. The sedimentation rate is elevated and there may be a leukocytosis. Studies of the sera from patients with actinomycosis have revealed agglutinins, opsonins, precipitins, and complement-fixing antibodies. These criteria have been reported as having been successfully used in the diagnosis of the disease. Their continued use as a diagnostic procedure, however, has not met with much enthusiasm since the results are not too clear-cut to make them foolproof. The use of the fungous ex-

tracts for determining sensitization or hypersensitivity offer, on theoretical grounds, some hope for a specific cutaneous test; however, these have not been used sufficiently in humans to evaluate either the technic, the type of extract used, or the results obtained.

Histopathology—Microscopically, the lesions are granulomatous in nature. The specific lesion in its early stage consists of a small nodule of polymorphonuclear leukocytes with the fungus in the center of the node. There is an infiltration of lymphocytes, polymorphonuclear leukocytes, eosinophiles, and irregular large macrophages. The area in turn is surrounded by plasma cells and proliferating connective-tissue cells. The connective tissue surrounding the whole area becomes noticeably edematous and is infiltrated by leukocytes and lymphocytes.

As the organism grows, the bacillary forms develop filaments which become intertwined. The cells around the fungous elements show degenerative changes and are finally replaced by invading leukocytes. The result is a central area of fungous elements which are intertwined and compact and which may show either radiate or "club" formation or simply a mass of filaments. This is the granule seen in smears of pus. The edematous connective tissue appears as granulation tissue. Macrophages, many showing phagocytized fat, may be seen in the surrounding area, and some of these large cells may invade the pyogenic mass. It is this fat which is responsible for the yellow coloration seen grossly in lesions, especially in the liver. Several of the nodules coalesce to form large masses.

As this large necrotic area or abscess increases in size and forms a frank abscess, the pus seeks more space and consequently burrows through the adjacent tissue forming a sinus. The sinuses do not heal easily because of the constant flow of pus, with the result that numerous sinuses are formed, many becoming intercommunicating. Large pus pockets develop along the path of the sinus which eventually becomes filled in with granulation tissue showing scattered leukocytes and newly formed blood vessels

with young connective-tissue cells. The characteristic finding is the granule. Although to an experienced investigator, the lesion, in the absence of granules, may suggest actinomycosis, an exact diagnosis would necessitate the finding of the fungus.

Mycology—The fungi of actinomycosis may be divided into two main groups, the aerobic and the anaerobic or microaerophilic. The aerobic forms, which some workers regard as a distinct biologic group and, therefore, classify as *Nocardia*, as exemplified by *N. asteroides*, is made up of both pathogenic and saprophytic organisms, some having acid-fastness as a property. The second group, the anaerobic or microaerophilic Actinomyces, is considered as being made up of a single species, *A. bovis*, or as preferred by some, *A. israeli*. This is the commonly encountered pathogenic actinomycete in human tissue which is gram-positive, and non-acid-fast, is chiefly responsible for the so-called "sulfur granule" and is found in approximately 90 per cent of the cases of actinomycosis. In tissue or pus Actinomyces or *Nocardia* produces granules with or without club formation which may be either white, yellowish-white, black, green, or red.

GRANULES may be found by either collecting the draining pus in a sterile test tube and examining before a bright light for the small opaque masses of mycelium or by expressing the pus from the lesions by exerting pressure on the sides of the sinus. In freely flowing pus the granules are usually found with ease. Granules may also be found on sterile dry gauze pads left on the open sinus overnight. When not found in the pus, granules may sometimes be obtained by curetting the walls of the sinus. Sputum should be thinned out in a petri dish and may be examined under a dissecting microscope for granules. Granules are not often seen in sputum and are rare in spinal fluid; consequently one must look for gram-positive or acid-fast bacillary or branching filaments.

When Actinomyces first invades human tissue it does so either in the form of a bacillus-

like cell, approximately 0.2 to 0.6 microns in diameter and somewhat irregular in form, suggesting diphtheroids, or as nonseptate, occasionally branching filaments which vary in length and are approximately 15 microns. The fungus is carried through the blood or lymph streams and comes to rest at some locus which, if it be favorable for growth, allows the organism to grow and multiply. The bacillary form or the filaments elongate, branch, and become intertwined and compact to make up the young granule.

The growth process continues and develops, resulting in one of two types of granules, the soft or hard. The soft granule may be seen as a mass of intertwined filaments with degenerate leukocytes in the center and peripheral extensions. The young hard granule likewise consists of intertwined hyphae, but extending from the periphery, in the form of rays and usually covering the whole granule, is a hyaloid or gelatinous-like substance which appears to engulf the fungous filaments with the terminal portion either filiform, flattened, or, usually, swollen or club shaped. These formations give the organism the name "ray fungus." When the granule is older and it is placed on a glass slide, it is usually resistant to crushing, often causing the cover-slip to be broken. These older granules have the consistency of small calcified nodules. When examined microscopically they are seen to consist of lobulated masses. The central area is amorphous while the lobulated periphery is hard, glasslike, refractile, and radiate, with a yellowish tinge. When stained with hematoxylin and eosin, the central area and the surrounding amorphous material consisting of intertwining filaments and degenerate cells stain heavily with hematoxylin. The periphery of the granule consisting of the rays, stains with eosin and is said to be acidophilic. When stained by the Gram-Weigert method, the fungous filaments are gram-positive, while the clubs take the eosin stain.

The final step in the making of a complete diagnosis is the cultivation of the granules to determine the species of fungus involved. Since it is difficult to tell whether the organism

is aerobic or microaerophilic, media satisfying the needs of both types should be employed. When the material is unlikely to be contaminated, as in the case of spinal fluid, cultures are obtained by making the inoculations in deep tubes of beef or veal infusion broth. Some of the material should also be streaked heavily on several tubes of Sabouraud's glucose agar. Sputum, draining pus, and sinus-wall scrapings should be inoculated into veal infusion glucose agar shake tubes and streaked on Sabouraud's glucose agar slants. Other media may also be used, but these are the media most commonly used in laboratories and give good results.

The microaerophilic *Actinomyces bovis* or *israeli* is found at the bottom of the broth cultures as small, creamy white, flocculent colonies which break up easily on shaking. In the veal infusion shake tubes the colonies appear in three to four days as a band of small, discrete or confluent, lobulate colonies approximately 5 to 10 mm. below the agar, with larger colonies distributed in small number at various levels of the medium. Individual colonies, when examined on a slide, show fine branching filaments and small bacillary and coccoid forms which are gram-positive.

Aerobic strains, such as the so-called *Nocardia asteroides*, when grown on Sabouraud's glucose agar usually produce glabrous, verrucous, irregularly folded or convolute colonies which vary in color. *N. asteroides* starts as a pale yellow growth and becomes deeper in color with age. *Actinomyces* or *Nocardia madurae* develops as small, longitudinally folded, discoid, crateriform, yellowish-white colonies becoming waxy and changing to a pink and then red color. When examined microscopically, the colony appears to be made up of fine branching hyphae approximately 1 micron in diameter. There are numerous pathogenic species of *Actinomyces* and/or *Nocardia*, many of which may be variants of those described. There are also numerous nonpathogenic or saprophytic aerobic *Actinomyces*, and their nonpathogenicity may be determined by the intraperitoneal inoculation of guinea pigs with negative results.

Differential diagnosis—The multiformity of clinical characteristics of actinomycosis, as has been described, suggests a number of disease entities which should be ruled out. The elimination of other infectious processes depends chiefly on the finding of the pathogenic fungus. Usually the clinical picture may be pathognomonic. Diseases which may be confused with actinomycosis include tuberculosis, syphilis, carcinoma, and many other mycotic granulomas such as blastomycosis, coccidioidomycosis, sporotrichosis, and paracoccidioidal granuloma or South American blastomycosis, typhoid fever, amebiasis, osteomyelitis, glanders, tularemia, granuloma inguinale, chronic appendicitis, intestinal carcinoma, sarcoidosis, sarcoma of the retroperitoneal tissue or iliac bones, psoas abscess, brain tumor, and liver abscess.

Treatment—In the past, the treatment of actinomycosis has not been too favorable. The localized and well-circumscribed lesions had a good prognosis, but systemic infection, of long duration, was, in most instances, a fatal disease. Present-day methods, however, have brought about radical changes in the therapeutics of actinomycosis so that with the exception perhaps of the well-advanced cases with invasion and destruction of brain tissue, one may well hope for recovery.

OLD MAINSTAYS in the treatment of actinomycosis have been iodine and its salts, potassium and sodium iodide, copper sulfate, thymol, vaccines, roentgen rays, radium emanations, and surgery. Potassium iodide is given as a saturated solution starting with 15 drops three times a day orally and increased 5 drops daily to the point of tolerance. Sodium iodide may be substituted for potassium iodide and given intravenously in daily doses of 1 gm. Tincture of iodine is given in milk or water starting with 5 drops three times a day and increasing the dose to tolerance. The iodides seem to be of extreme value when given as an adjunct to other forms of therapy but have not proved to be effective when used alone. Thy-

mol, 1 to 2 gm. daily by mouth on an empty stomach, or 10 to 20 per cent in olive oil applied locally or injected into sinuses, has given good results in some cases. Copper sulfate in $\frac{1}{4}$ grain doses by mouth and colloidal copper injections at four to seven day intervals have given good results. Vaccines have been of value in 55 per cent of cases, chiefly of the cervicofacial type, and in another series of 23 patients when used in a dosage of 5 to 10 million mycelial fragments. Roentgen rays and radium emanations have been effective in localized cases but are of little or no value in systemic involvement, except perhaps in the case of indolent lesions. Roentgen irradiation may be of great value as a supplement to other forms of therapy, particularly surgery.

UNDOUBTEDLY, surgical drainage is advisable and, in fact, essential in most cases. With the administration of the newer chemotherapeutic agents, the surgeon is in a better position to do more radical surgery. Sinus tracts should be drained, and débridement or excision of the severely damaged or diseased tissue should be accomplished where and whenever possible. Pulmonary lesions may drain through the bronchi, but pleural lesions often require surgical intervention. In a few cases, lobectomy or pneumonectomy have been performed with good results when all other means seemed hopeless. On the other hand, surgery without the additional use of chemotherapeutic agents may be dangerous unless the procedure is sufficiently radical to eliminate all signs and traces of the infectious process.

The sulfonamides have proved to be very effective in the treatment of actinomycosis. These have been used in dosages beginning with 2 gm. as the initial dose, and then 1 gm. every four hours or four times a day. Sulfanilamide, first used in 1938, was effective in cases caused by either the aerobic or microaerophilic Actinomyces. The British have preferred sulfapyridine either in small doses or in large doses. They claimed better results when the drug was used by the intermittent method, 1 or 2 gm.

four times a day for four days, followed by four days of no treatment, and repeating the cycle until the lesions showed evidence of clearing, when the drug was either discontinued or the dosage cut down. In America sulfadiazine is the sulfonamide of choice. The drug is given 1 gm. every four hours so that a good level in the blood is obtained. This is continued until the lesion shows evidence of clearing, and then reduced so that a level of 5 to 10 mg. per cent in the blood is maintained. British workers favor a short treatment period, whereas Americans prefer a more cautious course extending over a longer period.

The therapeutic value of penicillin in actinomycosis, I believe, has been amply demonstrated. Dramatic results have been obtained in a few days with doses as small as 5000 units given every three hours, preferably by the intramuscular route, while in others the dose has been considerably higher. Penicillin seems effective in controlling severe toxic symptoms in extensive actinomycosis cases. Excellent results were obtained by treating primary cutaneous actinomycosis with 5000 units of penicillin every three hours with a total of 410,000 units of penicillin. Some cases have responded dramatically on large doses of penicillin, given intramuscularly, following sulfonamide therapy. Prolonged treatment seems to be advocated.

The choice of treatment would seem to depend, therefore, on the location, type, duration, extent, and severity of the lesion. For isolated lesions, one form of therapy may be adequate; for the advanced cases, however, a combination of several forms gives best results. A good plan of procedure in the light of our present-day knowledge, once the diagnosis is established, would be to place the patient on an adequate diet supplemented with vitamins and iron along with bed rest in order to help the body build up its natural resistance. Treatment with penicillin should be started immediately, 50,000 units, intramuscularly, every three hours. A sulfonamide, preferably sulfadiazine, should be given starting with 2 gm. and then 1 gm. every four hours. Unquestionably, surgical procedure is of great importance. Except

for such cases where immediate surgical intervention would appear to be necessary to alleviate pressure, pain, or discomfort, it would be wise to wait until a sufficient number of doses of the chemotherapeutic agents have been administered to produce a satisfactory level in the blood and consequently avoid the possibility of spreading the infectious agent and the resultant process.

When and if surgical drainage and excision of infected tissue have been carried out, the chemical agents should be continued postoperatively until the signs and symptoms of the disease have been greatly diminished or eliminated, and then the dosage should be reduced. Roentgen irradiation may supplement therapy, as may potassium iodide. In the event of sensitivity to the drug or drugs, one or both may be discontinued or reduced temporarily and then reinstituted. When the patient appears to be clinically well, one of the drugs should then be given prophylactically by mouth. For this purpose, sulfadiazine may be adequate, 1 gm. four times a day and then reduced to 1 gm. three times a day and maintained for at least two months. With the present day tablet form of penicillin, this drug may be used. Potassium iodide has been used as a maintenance drug. In the event of recurrence of lesions, large doses of penicillin should again be given.

SPOROTRICHOSIS

Definition—Sporotrichosis is a granulomatous disease process which may be subacute or chronic and is usually confined to the cutaneous or subcutaneous tissue. The organisms, members of the genus *Sporotrichum*, may spread through the lymph channels to produce a multiplicity of clinical forms involving the skin, internal viscera, bony structures and the cerebrospinal system.

Clinical manifestations—The clinical course of sporotrichosis is much like that of other mycotic granulomas. The disease manifests itself in various forms affecting the skin, cutis and subcutis, and may spread systemically. For purposes of general classification, sporotrichosis

may be divided into three main groups which include lesions of the epidermis, dermis, lymphatics, mucous membranes, bones, and internal organs and structures.

It is interesting to note that many of the primary lesions of sporotrichosis follow trauma with infection setting in. Animals, fowl, birds, vegetation, and various insects have been reported as carriers or vectors. The disease may also be contracted by the handling of contaminated dressings from open lesions of the disease.

Group I consists of localized sporotrichosis, which may be either cutaneous or subcutaneous. In the cutaneous form there are seen nodules, ulcers, gummas, and abscesses. The skin lesion may be localized, or it may become progressively extensive. The primary lesion may begin as a small abscess, usually at a site of trauma. The abscess enlarges to form a nodule, which is at first hard, elastic, freely movable, and nontender and then becomes attached to the skin which becomes pink in color, then purple. The nodule forms a fluctuant center and then ruptures spontaneously. The purulent material exudes onto the surface of the skin and may cause the formation of secondary lesions. The original lesion may close and heal spontaneously or it may ulcerate and become black, to produce what is called a sporotrichotic chancre; this may persist for months. These lesions may also become granulomatous and form a gumma. Cutaneous involvement may also be seen as nodular, crusted areas, infiltrated plaques, verrucous or papillomatous lesions, and papular and follicular patches. Such lesions closely resemble epitheliomas, verrucous tuberculosis, papulonecrotic tuberculids, sarcoid, and syphilids.

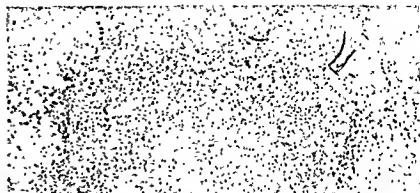
THE sporotrichotic chancre may serve as a primary focus from which, after a few days or weeks, the fungus spreads through the lymph channels to produce a chain of secondary subcutaneous nodules. This is the localized subcutaneous lymphatic involvement type of sporotrichosis. The secondary nodules are at first freely movable, but then become attached

to the overlying skin. The ascending nodules and the infectious process develop painless, cordlike thickening of the lymphatics. The nodules soften and finally ulcerate, discharging a small amount of thin pus. The nodules seldom involve the larger lymph nodes of the axilla; this is an important diagnostic point in the differentiation from tularemia, in which the lymph nodes are usually involved. Sporotrichosis of the localized lymphatic type rarely becomes disseminated through the lymphatics or through the blood stream to other parts of the body. The primary lesions usually heal, but the secondary gummatous lesions, if untreated, may persist for months.

Gummatous, disseminated sporotrichosis—Group II—Consists of several types: the non-ulcerating, gummatous forms; ulcerating, disseminated, subcutaneous sporotrichosis, which include the tuberculoid, syphilitic, ulcerating, polymorphic, and furuncle-like types; large multiple, disseminated abscesses; mixed forms, including polymorphic gummas, large abscesses, secondary lymphatic lesions, and dermic and epidermic involvement. These forms are rare in America.

Group III, classified as extracutaneous forms or systemic sporotrichosis, includes involvement of the mucous membranes, lungs, muscles, osseous structures, joints, synovial membranes, gastro-intestinal tract, cerebrospinal system, and other internal viscera and organs. These may be, and usually are, associated with primary or secondary cutaneous lesions.

Lesions of the nose suggest rhinitis, whereas infection of the mucosa of the oral cavity suggests stomatitis, glossitis, laryngitis, and angina. Lung involvement is rare, but the patient usually complains of many "colds" associated with a cough productive of purulent mucus. Roentgenologically, the chest may show extensive infiltrations throughout both lungs with a moderate decrease in aeration suggesting atypical tuberculosis, syphilis, or a fungous infection. Bone involvement usually appears as osteoperiostitis or hypertrophic osteitis. The tibiae, which are most frequently involved, develop spontaneous fractures.



(Top) Characteristic growth of *sporotrichum schenckii* on Sabouraud's glucose agar slide culture. Note conidial formation on lateral appendages. X 1360.

(Center) Sporotrichosis with lymphatic spread. Note nodules indicated by arrows.

(Bottom) Sporotrichotic nodule in upper third of cutis. This is a characteristic granulomatous nodule. Methylene blue and eosin stain. X 135.

Diagnostic procedures—The correct diagnosis of sporotrichosis, as in all other mycotic infections, depends upon the demonstration of the causative fungus. Serological methods, like those in actinomycosis, are not always reliable. Fungous suspensions are not standardized, and positive tests obtained by complement fixation or by the agglutination test may not be specific since they often are false positives. The intracutaneous test, using a suspension of dead fungi injected intramuscularly in the forearm, may likewise produce false posi-

tives. In the clinical laboratory the only significant finding is the presence of a moderate eosinophilia in the blood and a large number of eosinophiles in pus from nodules.

INOCULATION of animals as a diagnostic procedure may be used successfully when pus aspirated from unruptured nodules is injected into male mice or rats intraperitoneally or intratesticularly. The animal will die in approximately nine to twenty days with a severe orchitis, and at necropsy there may be seen extensive involvement of the lungs, liver, and other organs. Smears of pus or sections of tissue stained by the Gram-Weigert method or by the Unna alkaline or polychrome methylene blue technic will reveal the gram-positive or blue cigar-shaped or oval cells of *Sporotrichum*, either intracellularly located or freely dispersed, in clumps, in the tissue.

Histopathology—Sporotrichosis, as has been described, is characterized by the production of various types of skin lesions and of systemic involvement. Such lesions consist of gummas, ulcers, furuncle-like types, abscesses, nodules either with or without lymphadenopathy, and a general granulomatous response in the skin, internal viscera, or bony structures. The microscopic response varies according to the type of lesion present. In general, however, there is inter- and intracellular edema in the epidermic layers associated with an irregular acanthosis, extensive or moderate, and, at times, suppurating foci, which are particularly evident in the ulcerating type of lesion. There is a prominent infiltrate of polymorphonuclear leukocytes scattered throughout the pseudoepitheliomatous growth in the cutis forming micro-abscesses in some regions. In addition, the infiltrate in the cutis may consist of plasma cells, young connective-tissue cells, many epithelioid cells, lymphocytes, some mast cells, and giant cells of the Langhans' type. The lymph spaces in the upper third of the cutis are usually dilated.

The granulomatous nature of the lesion is emphasized by the nodular formation. These

nodules may be superficial or deep in the cutis. The center of the nodule usually shows necrotic masses or small abscesses, the chronic suppurative zone, and this area is surrounded by richly stained cells consisting of polymorphonuclear neutrophils, eosinophiles, lymphocytes, red blood cells and macrophages. Closely adjacent to this area is the tuberculoid zone which consists of many epithelioid cells and giant cells, varying in number, size, and shape and often arranged in tubercle-like fashion. The peripheral or outer area of the nodule, the syphiloid zone, is made up of a rich cellular infiltrate of young connective-tissue cells, lymphocytes, plasma, and mast cells and an increased number of blood vessels simulating a syphiloid appearance.

Unfortunately, fungi are rarely demonstrated in tissue or in pus with any of the standard methods of staining. Since the histopathology of sporotrichosis may have the characteristics at times of a granuloma, other times of tuberculosis, and still again those of syphilis, one cannot rely upon microscopic tissue observations to make a correct diagnosis.

Mycology—The best, safest, and surest way of diagnosing sporotrichosis is to find the causative *Sporotrichum*. Although it is very difficult to find *Sporotrichum* in tissue or pus, on occasion these cells may be seen. They consist of short, blunt, rodlike or fusiform, somewhat rectangular, basophilic forms measuring 1 to 3 by 2 to 5 microns and occurring singly or in groups. Ovoid to spherical cells may also be seen, and all these cells may be found either freely dispersed in the necrotic material or phagocytized by mononuclear leukocytes or macrophages. The cells are gram-positive and have a capsule-like, colorless periphery. Another structure, described as the asteroid form, consisting of a central cell of *Sporotrichum* with peripheral, radiating extensions analogous to the ray forms seen in actinomycotic lesions, may rarely be found. The fungus *Sporotrichum schenckii* may be responsible for all these structures.

Since it is so difficult to find the character-

istic cells of *S. schenckii* in pus or tissue, one must resort to the culturing of the fungus on artificial mediums. For this purpose, unruptured, subcutaneous nodules are aspirated with a sterile needle, and the contents of the syringe expressed or streaked on Sabouraud's glucose agar slants, some of which are incubated at 37° C. and others maintained at room temperature. The organism grows faster at incubator temperature and appears on the second to third day as small, pin-point colonies at first white or cream-colored, becoming light to dark cinnamon and black when fructifications develop. As the fungus grows, the growth becomes moist, and the colonies become confluent to take on a cerebriform or vermiculate appearance. Giant colonies of *S. schenckii* may vary in color, being either light cream, gray, or black. Such color variations have little significance with *S. schenckii* since the same strain may go through these color changes.

MICROSCOPICALLY, the fungus is seen as a growth of tangled, interlacing, filamentous mycelium, the hyphae being approximately 1 to 5 microns in diameter, depending on the type of medium used. Conidia are many, spherical, ovoid, or pyriform, pedicellate or sessile, and grow singly or in groups, measuring approximately 2 to 4 by 2 to 8 microns and are found laterally or terminally. Oidoid cells may form singly with budding or may develop into chains of spherical, ovoid, or arthrosporous cells.

Differential diagnosis—The diagnosis of sporotrichosis is relatively easy in the lymphatic type since the clinical features may be pathognomonic. The chain of nodules following along the lymph channel and originating from a primary focus on a finger, the hand, or wrist following a trauma should, however, be carefully differentiated from tularemia or glanders. Nodular leprosy should be ruled out. Squamous cell carcinoma may spread by way of the lymph channel and present a similar picture. In such instances, a clinical diagnosis of sporotrichosis may be entertained. The nodules of squamous

cell carcinoma, however, are not freely movable, are more infiltrated, and are not fluctuant as are the nodules of sporotrichosis. Localized lesions that may become ulcerative, nodular, or gummatous simulate a neoplasm as well as syphilis, tularemia, mycotic granulomas, or cutaneous manifestations of idiosyncrasies to drugs. Generalized lesions likewise may easily confuse the examiner, and syphilis especially should be ruled out.

Treatment—Fortunately, sporotrichosis, except perhaps for the rapidly spreading or fulminating, disseminated type and some of the systemic forms, is not usually a fatal disease. Surgical treatment in the form of incision, excision, curettage, or actual cautery is contraindicated since such procedures induce more suppuration, prolong natural healing tendencies, and consequently retard rather than effect a cure. Roentgen ray therapy applied locally as an adjunct to other forms of therapy may be useful, but in general the results from x-rays alone are not encouraging. Vaccine therapy may have its uses but as yet has not proved its value.

Potassium iodide is practically a specific in the treatment of sporotrichosis. The treatment of choice is an aqueous saturated solution of potassium iodide given orally beginning with 10 or 15 drops in water or milk three times a day. The dose may be increased as much as 5 drops total increment daily until the point of tolerance is reached and then maintained at the maximum dose. Patients may often tolerate large doses, as much as 350 drops three times a day, but this varies with the individual patient. If the patient does not tolerate potassium iodide orally, responding with indigestion, sodium iodide may be given intravenously. Locally, wet dressings of Burrow's solution (1:15) or Lugol's solution, half strength, or ointments containing up to 5 per cent iodine or 6 per cent bisnuth tribromphenate (xeroform) in white vaseline, may be applied. The iodide by mouth should be continued for at least six weeks after the lesions have apparently healed to avoid the possibility of relapse or recurrence.

Leprosy, Its Detection and Management

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THE diagnosis of leprosy in its advanced stages is easily made by the physician or layman familiar with the illustrations of the disease to be found in textbooks of medicine. Leprosy, with most of its manifestations presenting themselves superficially, need not be a process difficult to recognize, and usually is not if given consideration in differential diagnosis. It may be missed, through oversight, in light cases with lesions of limited extent. In spite of the fact that leprosy is extremely variable in its appearances, there are hallmarks, one or another of which is so uniformly present that recognition is easy.

Leprosy is a fiercely chronic affair. It is exceptional for a recovered individual or an arrested case not to be left with evidences of the past process. It is a disease which may progress steadily and slowly from its beginnings, or it may advance rapidly during periods of acute activity, with other long periods of slow remission intervening. What the physician sees in a given case at a given moment is a mixture of old processes, perhaps some of them obsolete,

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with the fresh and new, and some elements of both are commonly present.

Little is known of the pathogenesis of the process from the time of infection to the appearance of recognizable lesions. An incubation period of five years or more is usually accredited, yet careful and correct histories often show that the very earliest signs and symptoms, often mild and transient, followed exposure by no great period of time. As a rule, leprosy is a generalized infection when first recognizable. There are exceptions recorded, sufficient in number to have raised the question of the possibility of the occurrence of a primary focus, as in tuberculosis. The transmission of leprosy by cutaneous inoculation is seen but rarely in adults. In most cases it is usually assumed that when exposure has been heavy and prolonged, bacilli have entered the body by every possible port.

The earliest visible lesions of the skin are usually accompanied by demonstrable neural changes, and vice versa. Although cases are seen with severe nerve damage and no lesions of the skin, these are usually old cases in which the cutaneous lesions, never more than mild, have vanished. So-called neural leprosy, actually only infrequently seen in its pure form, is



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leprosy in which the infection or damage to the nerve persists while changes in other tissues recede.

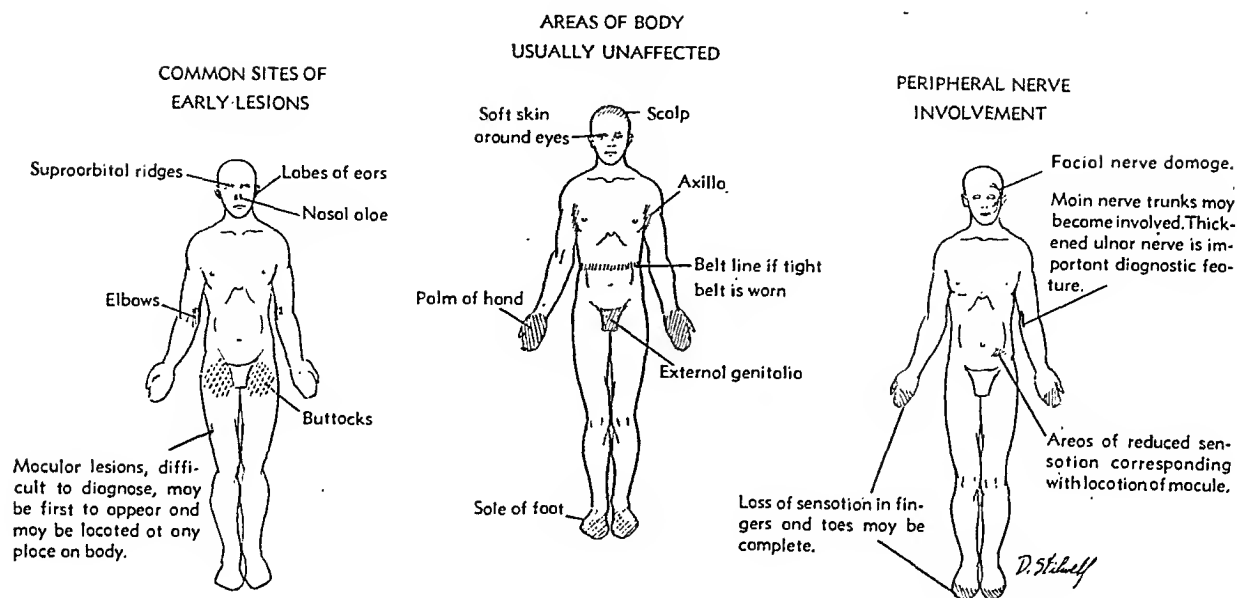
Involvement of tissues other than the skin and peripheral nerves occurs most commonly as cases advance. The regional lymph nodes are always involved, though usually to a moderate degree only. The nose and throat are often severely damaged. In males an interstitial leprosy orchitis develops in the large majority of cases eventually, and although severely damaging to the reproductive tissues, is commonly not apparent clinically. The eye is affected in almost 90 per cent of cases. Visceral lesions of the liver and spleen, consisting at times of enormous numbers of very small foci, are most variable in their bacillary content, and, although clinically they do these organs little or no damage and are autopsy findings rather than clinical observations, they play their part in the disease. Other viscera are not directly injured by the infectious agent. One of the curiosities of leprosy is that while it does severe damage to periph-

eral nerves, the central nervous system and visceral nerves are never touched. Even in the eye, which is often infected by way of the blood stream, the optic nerve escapes completely.

The early lesions of leprosy may appear on any part of the body, but there are some areas of predilection and other areas which are almost never touched. The buttocks are a common site of early lesions, as is the skin over the elbows, both of which sites may easily escape notice. The nodular lesions of the face are often seen earliest in the supra-orbital ridges, with falling of hairs from eyebrows. The lobes of the ears and alae nasi are commonly infiltrated from the beginning. In the early stages the lobes of the ears may present little more than a "doughy" consistency, and the cheeks may show an increased thickness and inelasticity to palpation, without visible alteration, owing to the leprosy infiltration present in the dermis. It is often said that the "exposed" surfaces of the body are those most often involved, yet the hands and feet suffer more severely from the effects of nerve damage than from immediate involvement of the skin, and the palms and soles rarely show leprosy infiltrations. Other areas which commonly escape are the axillae, the external genitalia, the skin immediately around the eyes, the belt line in the man who wears a tight belt, and others. Lesions commonly end abruptly at the line of the scalp.

THE simplest form of leprosy lesion is the "macule." These may appear originally as fairly broad lesions, not in any site of predilection but anywhere on the body, and exhibit themselves in a variety of colors—reddened, depigmented and white, or even hyperpigmented. Although these macular lesions may go on to develop into lepromatous nodular formations in broad plaques, it is often only at their borders that the lesions continue active with the building up of thick infiltrations of all layers of the skin. The lesions are composed of granulomatous infiltrations along all the structures of the skin containing huge numbers of lepra bacilli. Some spreading at the borders

CLINICAL DIAGNOSIS OF LEPROSY



may occur, but there is no rule. The central part of the macule usually becomes inactive and loses most or all of its bacilli, yet the histologic changes seen in the macule—with the exception of the tuberculoid lesions—differ from those of the nodule only in degree, extent, and status of activity. They are identical in character.

The importance of the macular lesions lies in the fact that they are often the earliest lesions and often escape correct early diagnosis. Actually their designation as "macular" is inexact, because some slight thickening and infiltration of the skin accompanies them. There are various clinical variations from the so-called simple macules and neuro-leprids to tuberculoid macules with fine papules distributed through them, having a quite different histologic character. The bacillary content of macular lesions is most variable. Bacilli may be present only transitorily, or, on the other hand, they may be present in astonishing quantity in view of the slight involvement of the skin. Even the most faintly visible lesions may show organisms in surprising quantities. In the tuberculoid varie-

ties bacilli are extremely scarce, and frequently their demonstration is impossible.

The further development of the individual case of leprosy is variable in the extreme. Leloir's dictum of 1885¹ that "there is only one leprosy, infinite in its varieties," is not changed by the fact that no two cases are precisely the same, and that "unusual" cases are so common that classification into clinical types does not always succeed. Because there are a dozen patterns which are repeated in any large group of cases, and because some varieties are common in one country and rare in another, it has been frequently suggested that factors such as race, diet, heredity, climate, and social habit are determinants, or that different strains of the infecting organism produce different clinical types. While these possibilities exist, proof thereof is lacking. On the other hand, there has been an increasing fund of information which indicates that little-understood factors of resistance, native and acquired, or even partial cross-immune reactions with other infectious agents, play a significant role.

Daniellsen and Boeck,² ninety-nine years ago, divided leprosy into the nodular (tubercular)

and the neural forms. There is, however, no case of leprosy, not even of the most pure neural type, in which there has not been some cutaneous change at some time, however fugitive it may have been. The reverse is equally true. Even in those uncommon cases of leprosy which exhibit no neural changes under examination, anatomic studies show some changes in nerves

with those of the face and trunk. The most dramatic changes in the extremities are due to nerve involvement, and not to actual leprous invasion of the tissues; the nodular and neural changes do not so much overlap in the hands and feet. The skin of the lower parts of the leg often undergoes a peculiar change, partly due to the residue of former macules and partly to

HISTOLOGICAL CLASSIFICATION OF LEPROSY

TYPE	ORGANISMS	LEPROMIN REACTION	PROGNOSIS		DISTRIBUTION IN PER CENT	
			With Treatment	Without Treatment	World	United States (Carville)
Lepromatous	Numerous	Negative	Poor	Improvement	50-80	65
Intermediate	Variable	Variable	Variable	Good	20-40	33
Tuberculoid	Most rare	Positive	Excellent	Excellent	10-30	3

NOTE.—Neural changes occur indiscriminately in nearly 100 per cent of all cases.

regional to the lesions.

Too much emphasis cannot be put upon the neurologic changes from the standpoint of diagnosis. On the trunk, areas of anaesthesia roughly corresponding to the macular formations can be readily demonstrated. Sensation in these areas is almost never totally lost because the worst damaged nerves usually contain a few unaffected nerve fibers. Diminished sensation is shown by the inability to distinguish hot from cold, or sharp from dull; because the damaged nerve has a limited ability to regenerate, some part of the loss in sensation is permanent. In the extremities, the loss of sensation is usually more striking. The bacillary invasion of the nerves spreads upward, and in time whole main trunks become involved. Loss of sensation often becomes total in the fingers and toes and is accompanied by atrophy of the muscles and bones of hand and foot and contractures of the fingers. Palpably thickened ulnar nerves above the elbows are an important diagnostic feature.

It is in the more distal parts of the extremities that the trophic changes of leprosy occur. Although lepromatous changes may take place in the hands and feet, they are slight compared

loss of nerve supply. It becomes somewhat ichthyotic and is sometimes discolored or sclerodermatous; trivial injuries may lead to the formation of large chronic ulcers. Fungus infections of the nail-beds are common, and the added atrophies of phalangeal and metacarpal and metatarsal bones often lead to crippling deformities. It is probable that, although the large blood vessels are too rarely directly involved in leprosy to be a factor, some loss of the neurovascular mechanism is a large contributing factor in the trophic changes.

The diagnosis of leprosy is more often missed from failure to consider the neural aspects of leprosy than from any other cause. Patients will tell, but not complain, of loss of sensation or paresthesias, and areas of diminished sensation can often be shown far beyond the patient's suspicion.

ALTHOUGH classification of leprosy into clinical types has always been useful, in late years it has been found that classification from a histologic standpoint yields information of great value. Although complete agreement on details is still wanting, there is increasing reali-

Although our knowledge of the epidemiology of leprosy leaves much to be desired, evidence of transmission by direct contact can be found in a majority of cases. In the endemic areas in the United States eradication of the disease is unlikely without some greater and more deliberate effort at case-finding, a procedure which calls into play all the fine knowledge of the disease one can muster, and all the intelligent and sympathetic treatment of mankind of which the physician is capable. Leprosy has such a bad name and feared reputation that successful handling requires complete accuracy in diagnosis and skilled diplomacy on the social side.

The treatment of leprosy in this country has long since passed out of the stage of the medieval leprosarium, which was but a pesthouse, through the asylum stage of the nineteenth and early twentieth centuries, to the present-day conception of the leprosarium as a modern up-to-date hospital, as complete in facilities as it can be made. New York State, into which a moderate number of the world-wandering cases have filtered, has gone still further and made leprosy a disease to be treated on an outpatient basis. Other countries, especially those in which the incidence is high and the economic status low, adopt mixed programs, isolating cases only when bacterioscopically positive, and offering specific treatment extensively in special clinics. The handling of leprosy in this and other countries is not, and should not be regarded as, a permanently fixed procedure. Its future is particularly dependent upon what can be accomplished by treatment.

The management of leprosy is conveniently divided into three headings, specific treatment aimed at the primary infection, medical and surgical treatment of complications and intercurrent illnesses, and the economic, social, and public health management. It appears obvious that a specific treatment capable of arresting or even stabilizing the infection in the individual would have a profound effect on the other factors. It is even an open question whether any real progress can be made along other lines

without some method of limiting the damage done by the infectious agent.

Leprosy is by no means an invariably progressive disease. The tuberculoid cases do very well by themselves. Some 20 per cent of all cases under medical care become arrested and half of these remain arrested for life. In the absence of acute reactions or intercurrent illnesses, many cases tend to regress. The only "cure" of leprosy that is known is the permanent regressive phase.

It is the common experience that the new patient, when admitted to the adequately equipped institution, properly fed, rested, and generally medicated, improves for a period of some months thereafter. Granting that this is but a temporary improvement, it none the less makes the point that the general well-being of the patient, in the absence of a dramatically curative remedy for which there is no promise on any horizon, will always be an important factor in the treatment of leprosy, even as in tuberculosis.

The failure to recognize the common periods of regression as a normal feature of leprosy has led to innumerable wholly unjustifiable statements of the value of various therapeutic agents. The proper assay of the merits of any remedy must be made on a basis of years and not months. Selection of cases for treatment because they are particularly active at the moment of selection is certain to provide evidence of improvement in a majority, irrespective of the treatment given. No drug ever used has produced results better than those seen in cases of spontaneous regression. It is one of the unfortunate features of chaulmoogra oil therapy that much of the work done with this drug has not been subjected to satisfactorily controlled analysis.

No didactic statement of the value of intramuscular injections of chaulmoogra oil or its esters can be made on the basis of published reports. In British India, where the use of the drug has been most widely championed by Rogers and others and fostered for 25 years by

the British Empire Leprosy Relief Association, its use has not been found to have lowered the mortality or decreased the incidence. The present status of chaulmoogra oil may be said to consist of disparaging critical opinions from those who have used it comparatively little, opposed by favorable reports from those who have used it extensively in the absence of a better therapeutic agent.

There are other methods of administering chaulmoogra oil, notably the method of infiltrating the cutaneous lesions directly, one after the other, until the entire affected parts of the body are covered, omitting nothing. Cochrane, who has been doing this extensively in India, speaks of excellent results, not in the lepromatous cases, but in the intermediate group. The rationale of intramuscular injections of oils and their esters has always seemed debatable because of their absorption at a rate too slow to produce a therapeutically effective concentration in the tissues. Yet at best chaulmoogra therapy in leprosy seems inadequate as a final solution to the problem of treatment. Its future is not bright.

TREATMENT of leprosy with sulfones, promin and diasone⁴ was begun at the leprosarium at Carville five years ago on a semi-continuous basis; patients received intravenous injections of 5 gm. of promin 12 out of each 21 days, or 1 gm. of diasone 90 out of each 105 days by mouth. These treatments are continuing today, some patients having now received totals of more than 12 pounds of promin during the five-year period. To say that dramatic results have been obtained with either drug would be incorrect. There are no rapid cures, and six months are required to observe definite benefit of any kind. Yet the prolonged treatment with sulfones has been found to yield positive results in several ways. Patients under treatment seem to be largely freed of the risk of acute reactions, the appearance of new lesions is greatly cut down and eliminated in a majority of patients under treatment, and secondary infections are virtually absent. Under these con-

ditions the opportunity for the lesions to atrophy and regress is greatly enhanced, and this is precisely what takes place, at about the same rate as in examples of spontaneous regression without treatment.

It seems probable that the sulfones are sufficiently effective to dispose of the lesions of the small blood vessels in the leprous granulomas, which are forever casting bacilli into the blood stream, thereby leading to new lesions and acute exacerbations, but that they have no bactericidal effect whatever upon organisms in the tissue cells. It is probable that the sulfones are most effective in the atypical intermediate cases; however, good results are also seen in lepromatous cases, with the infection being stabilized rather than cured. The use of sulfones offers a definite advance over chaulmoogra therapy, but it is still a long way from being the final answer. Whether some of the newer antibiotics, such as streptomycin, will prove either effective or practical is a subject presently under investigation.

The complications of leprosy are so numerous and frequent that more of the physician's time is given to them than to the primary disease. They fall into five main categories.

1. Leprosy as it advances does much damage to the nose and throat, destroying the nasal cartilages, soft palate, and epiglottis in some cases, with much deformity resulting. Some of this is due to actual leprous infection of the nasal and pharyngeal mucosa and some to secondary infections in damaged and deformed tissues. Obstruction to nasal breathing is common, and obstruction of the passage of air through the glottis is occasionally fatal. As a preventive, sulfone therapy has been found most valuable. The added benefits obtained from sulfonamides and penicillin treatment of the infections of nose and throat have aided enormously in this field. The tracheotomy days of leprosy are all but over.

2. The ocular complications of leprosy lead to blindness in many cases. The eye is damaged in many other cases from several causes: (a) The lid paralyses and resulting ectropions follow involvement of branches of facial nerves,

ment of the individual with leprosy, both during his illness and after it may have become arrested. Because of its very limited extent in this country, it appears to the public at large

as a very specialized problem which does not concern them. To the physician, however, it is along lines of medical progress that the greatest promise lies.

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MEDAL FOR MERIT TO PAULLIN

Dr. James E. Paullin, Atlanta, Ga., president of the Interstate Postgraduate Medical Association, was recently awarded the Medal for Merit by the President of the United States. The citation signed by President Truman specifies exceptionally meritorious conduct in the performance of outstanding services to the United States since 1943 while serving as honorary consultant to the Bureau of Medicine and Surgery of the Navy Department and as a member of the directing board of the Procurement and Assignment Service of the War Manpower Commission during a period when the solution of problems of vital importance to the successful conclusion of the war required the intensive and unremitting efforts of all concerned. By his self-sacrifice and the employment of his high professional prestige, his talents as a physician and surgeon, and his abilities for successful organization of professional groups, he rendered the most responsible, notable and distinguished service. To the Navy directly, through his contributions as honorary consultant, and to all of the armed services through his achievements with the War Manpower Commission, Dr. Paullin's advice and direction were of exceptional and invaluable aid and assistance.

Cancer of the Colon

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WE HAVE been provided with two very interesting cases for this discussion. They represent two lesions, one in the sigmoid and one in the lower rectum, both successfully operated upon. One also represents a series of complications which follow surgery in a number of cases in this type of operation.

Before I discuss these cases I should like to recall to your mind some salient facts about the most frequently occurring lesion of the large bowel, and I say the large bowel meaning the colon and excluding the rectum because hemorrhoids, of course, are the most frequent lesion of the rectum; but carcinoma is the most frequent lesion of the large bowel that engages the surgeon's attention.

I would remind you that the large bowel is actually a dual organ developmentally and functionally and that the pathological types of carcinoma occurring in the two sides differ materially, particularly in their physical forms, and therefore produce a definite type of symptomatology in the two sides, extraordinarily different in their manifestations.

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The right half of the colon, beginning in the middle segment with the small bowel around to the ampulla of Vater is developed from the midgut; the left half of the colon is developed from the hindgut. They differ anatomically and functionally. The right colon's function is absorption; the left colon's function is that of a storehouse. Absorption of liquids takes place relatively actively in the right half of the large bowel; it takes place practically not at all in the sigmoid, descending colon, and rectum, thus accounting for the total inadequacy of rectal feeding after the right half of the colon has been successfully removed.

Anatomically, there is a difference in circumference and in musculature of the two halves of the bowel, and for that reason and others as well, obstruction develops when a signet-ring carcinoma grows around the circumference of the left colon or the sigmoid particularly. On the other hand, the growths that invade the cecum and ascending colon are large, uniformly flat, and ulcerating, and are situated upon the lateral surface of a larger piece of bowel where obstruction is in no wise likely to occur. In a fairly long series of operations on the colon I have not encountered acute intestinal obstruction in a half dozen cases in the right colon, whereas I have found that acute intestinal obstruction, either from the presence of the



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growth encircling the bowel or from some ill-advised attempts at roentgenography by the introduction of barium by mouth, is a relatively frequent phenomenon in the left colon.

I think that during the war there were few new developments in the surgery of the colon, with the one exception that the Army introduced the principle of exteriorizing wounds of the colon without immediate resection, as a routine. A perforated colon with a machine-gun bullet that went through it in two places was exteriorized with or without closure of the opening, and practically every wound of any magnitude in the large bowel was exteriorized, the peritoneum closed around it, and resection not attempted until later or until closure had been done; whatever the indications were for surgery it was postponed until after rehabilitation and resuscitation had been accomplished. Thus, except for the widespread use of exteriorization for colonic wounds and the routine use of a colostomy in rectal wounds (and that is not

a new principle; I think that was done in the last war by good surgeons), I believe that surgery of the colon and the rectum remained relatively as it was when the war broke out.

I should like to emphasize that the diagnosis of malignancy of the colon—which, of course, depends first upon recognition of some lesion of the colon, and the accurate localization of this type of trouble—depends largely upon our radiologic colleagues. They should have a fair opportunity, I think, to make an accurate diagnosis without being hindered by insistence upon quick radiologic methods and without being forced, as they not infrequently are, to x-ray a colon which has not been emptied of its contents.

We have now reached the stage where internists rarely insist upon a gastric radiologic diagnosis except after the stomach has been emptied of its contents. We are not that far along in the radiologic diagnosis of colonic lesions, and it is not an uncommon thing at all to have a patient brought in with acute intestinal obstruction superimposed upon a malignancy low in the large bowel, the obstruction being produced by the oral administration of an opaque medium. That is not an uncommon thing at all, and it is a totally inexcusable and a totally unnecessary complication.

THE first patient, a female, came in with a history of bleeding from the rectum for a period of ten weeks, and the hemorrhage was a massive one. The blood was red—red blood from the rectum—and in large quantities. Blood from the rectum that is red makes one immediately suspect that the lesion is in the rectum or the left colon. However, in her case she had an extraordinarily good history of a gastric ulcer which had persisted over a long period of time but from which she had had no hemorrhage. Therefore, gastric radiology was done in her case first and revealed a negative stomach and a negative colon. That was before she was admitted to the hospital.

I think it is fair to point out again that the oral administration of barium is not of any value

in the diagnosis of colonic lesions. Colonic lesions must be recognized by the administration of barium enemas, and the barium enema must be given in a clean bowel and must be retained long enough for the pictures and the fluoroscopy to be accomplished.

When the patient came into the hospital with this massive hemorrhage, she was given a barium enema which revealed a large polyp about 3 cm. in diameter on a stalk which was in the sigmoid. This polyp was low enough down in the sigmoid so that it perhaps could have telescoped itself down into the upper rectum, but it was low enough to be found by proctoscopic examination. With a good-sized polyp like that on a stalk, one is confronted with the necessity of removing that polyp before one diagnoses accurately the underlying pathology. The patient was properly prepared for resection of the colon or for colotomy, both of which were subsequently done.

I should like to discuss fully the preparation of any colonic case or rectal carcinoma that is going to be resected. I consider that particular preliminary step probably as important as any other step in the series of events that leads to the removal of the growth. The old days of rushing a colonic case into the hospital and operating on it the next day are gone, I hope. After proper purgation and proper washing of the bowel we spend from five to seven days in reducing the bacterial content, eliminating the fecal material in the bowel, feeding the individual with a residue-free diet, balancing the blood chemistry, overcoming any hypoproteinemia with whole blood transfusions, and being sure that the nutrition is raised to as high a point as possible over this period, at the same time that dehydration is actively combated. I think that this principle is definitely recognized now in all hospitals and clinics.

This patient was explored and the polyp was found in the sigmoid. Because it was on a long stalk, the polyp was excised, and immediately the pathologist was asked to review the base of the stalk and the mucous membrane that was removed from the sigmoid at the point where it was fixed. His report showed what is

so frequently shown, that there were some neoplastic cells at this particular point. Immediately a segmental resection of the sigmoid was undertaken and an end-to-end anastomosis with a complementary cecostomy was done.

There, again, I think we find a trend that is developing rather markedly in colonic surgery, and that is the utilization of immediate anastomosis following resection. I think all of us are doing more and more one-stage resections with anastomosis and are gratified by the low mortality and the satisfactory results that follow.

With the preparation, the meticulous technique, and, shall we say, the early ambulation, this lady was out of bed on the third or fourth day, having dangled her legs over the side of the bed the next morning. Since the operation she has never had to have a cathartic or a purgative. She made an uninterrupted recovery.

THERE is one thing I neglected to say, and that is in the preparatory measures which are being undertaken I cannot bring myself to subscribe completely to the high merit of the sulfa drugs. Until I returned from the Army I had never prepared a patient by using any sulfonamides. I had never used them in colonic surgery at all. I had not because I thought that the sulfonamides were not sufficiently stable to know which ones should be used; they were constantly changing, and I thought I recognized a definite danger in the administration of these drugs routinely when we then had comparatively little knowledge of what they actually did. I think the danger of the widespread use of the sulfonamides has been borne out and that we all recognize it. Now that we have come to the use of sulfathalidine, which is apparently more of a bacteriostatic agent than the others and which has fewer toxic effects, I have been using it and I believe that it has not minimized my results but I hope has helped me some. I cannot agree with the thesis of some of my colleagues who are willing to compare it to iodine in exophthalmic goiter. I would not admit that yet, but I do think it has merit.

We have another case which emphasizes two or three points. This patient is a white male sixty-two years old who had symptoms referable to his rectum in January, 1943. His main complaint was a little incontinence. He would go to the toilet and did not feel he could empty his bowel completely. Then he would pass a little liquid stool and be incontinent. Although he had only an occasional bleeding, he was continually soiling his underwear, and that brought him to the surgeon's attention. No particular bowel habit changes were worth noting. However, he did have considerable quantities of loose fecal material passed following normal stools, which could hardly be called constipation.

He came in without any loss of weight, had a good appetite, and generally was in good shape, with the usual diagnosis of hemorrhoids having been made twice without proctoscopic examination. I think that proctoscopic examination is so essential whenever bleeding from the bowel occurs that it always should be done.

This particular growth was only about three inches from the anal margin. In my experience most growths of the rectum occur higher than that. I recently saw a survey of a large group of cases where 50 per cent of the growths were said to be within three inches of the anal orifice. My experience is that most of them are higher up than that and that they are nearer the top of the rectum or at the rectosigmoid. I like to consider the rectosigmoid a space about three inches long, about an inch and a half above the peritoneal fold, and an inch and a half below; that is where most of the growths that I see occur. On June 15, 1943, this man had a combined abdominoperineal resection in one stage.

In the consideration of the choice of operations for carcinoma, I find myself without enthusiasm for saving-the-sphincter-muscle types of operation. I have no sentiment about the sphincter. I think if it has to be sacrificed to give us better end results it ought to be sacrificed. Any operation for malignancy is a mutilating operation, and I know of no good reason for not sacrificing the sphincter muscle if it will

give us a better opportunity to save these individuals' lives.

I believe that the Miles' operation, which is a block dissection, as nearly as one can do it, of the pelvis and a removal of all the lymphatic glands in the vicinity of the growth by taking out the levator muscles and going well into the ischiorectal fossa is the operation of choice. I have never had the experience of which I hear some of my colleagues complain, that their patients tell them they would rather die than have a colostomy. My patients do not tell me this. They all want to live, and if I tell them that the colostomy is the best way to succeed in their ambition, practically all of them agree and a colostomy is performed.

IAM SURE that very few cases of carcinoma of the rectum metastasize downward through the lymphatics in the downward zone of spread. I know perfectly well that that is true in probably 1.5 per cent to 2 or 3 per cent of cases. This patient happens to be one of those cases. He has had two resections of his perineal wound in the last two years for nodules which recurred in his perineum, and he had a Miles' operation.

In my own practice this year I have had two cases, one done by myself and one done by another surgeon, of recurrence in the posterior vaginal wall in women who had had a combined abdominoperineal. This makes three cases that I have seen this year where this type of metastasis was found. These cases certainly do occur, but the important zone of spread is not particularly the lateral or the downward zone, but the upward spread of malignancy into the mesentery of the sigmoid. I do not think that the latter can be removed except by doing a radical Miles' type of operation, removing a large segment of bowel and all of the mesentery that one can get out, and establishing a colostomy. Until the end results show that more than 60 per cent of the total group of cases operated on survive more than five years by saving the sphincter muscle, I am content

to continue with the colostomy as we have been doing it.

The next patient I would like to present has a colostomy in the midline. One can put the colostomy there, or put it laterally, like Miles, or like Hirschman in Detroit, take out the navel and put it there.

DR. RANKIN: Does this give you any trouble?

PATIENT: No trouble.

DR. RANKIN: It moves once a day?

PATIENT: Twice a day.

DR. RANKIN: You clean it up—

PATIENT: Morning and night.

DR. RANKIN: You go about your business and work all the time?

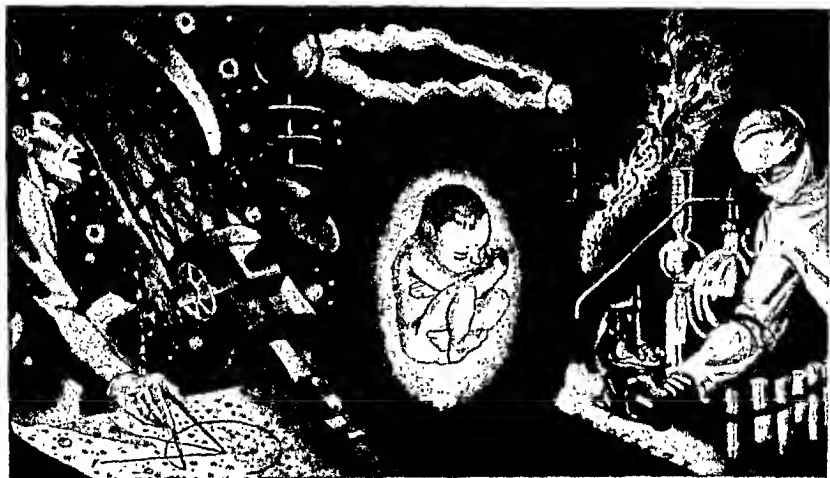
PATIENT: I have been working as a carpenter on the job.

DR. RANKIN: I would say that if a man can do that kind of labor without too much handicap, the colostomy is not bothering him.

PATIENT: I go on scaffolds thirty feet high, walking up the ladder.

DR. RANKIN: That is good. He has had a resection of his perineum twice for little nodules that have occurred there. It is perfectly smooth and clean now. There is no evidence of any recurrence and I think that he has had splendid results.

I want to reemphasize that a colostomy definitely is an unpleasant thing and is a small handicap, but it certainly does not necessitate social ostracism and it certainly does not keep people from carrying on their jobs.



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"THE SECRET OF LIFE" BY HARRY STERNBERG

Differential Diagnosis of Subacute Febrile Arthritis

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IN EVERY medical clinic there appears from time to time a patient with subacute febrile arthritis, the classification of which affords considerable difficulty to the attending physician. Some of these patients eventually leave the hospital without an etiological diagnosis and without achieving complete relief from their symptoms. It is therefore important for the clinician to make use of every possible diagnostic measure in the proper cataloguing of these cases. Without accurate diagnosis, rational therapy is unobtainable. The following case falls into this category.

In March, 1946, the patient, a girl nine years old, with no previous history of rheumatic disease, contracted a sore throat. Two weeks later she developed an erythema nodosum which affected not only the ankles but the legs and arms as well. Two weeks later she first noted pain and swelling of various joints, including fingers, wrists, shoulders, and hips. This syndrome was accompanied by fever which at first was of the low-grade type but later developed an intermittent quality with sharp daily rises to 102 or 103 degrees. Pain, swelling, and fever have persisted to the time that this paper was written. She was then suffering considerable pain in the left hip, probably because of spasmodic contractions of the muscles.

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A physical examination revealed a chronically ill young girl, who cries out frequently because of sharp pain in the region of the left hip. The throat shows nothing remarkable. The lungs and heart are negative. The abdomen is soft; the liver and spleen are not felt. There is no generalized adenopathy. There is no skin rash. The joints present the typical picture of rheumatoid arthritis with fusiform swelling of the fingers, thickening of the knuckles, and swelling and tenderness in the wrist joints. The patient is unable to elevate the right arm above her head. There is marked limitation of motion in the left hip, most probably because of muscle spasm. There is considerable tenderness over the head of the left greater trochanter. The knees and feet are in good condition.

X-rays of the hands show considerable osteoporosis with haziness of the carpal architecture. There is considerable thinning of the interarticular spaces of the proximal interphalangeal joints of the fingers.

The hemoglobin count is 11 gm. The red blood cell count is 3,700,000. The sedimentation rate of the red blood cells was 56 mm. in one hour by the Westergren method. All agglutination reactions are negative. The electrocardiogram shows a P-R interval of 0.2 seconds.

This girl is suffering from typical Still's disease, or what we now prefer to call rheumatoid arthritis of the juvenile type. The negative heart findings, spiking fever, the chronically swollen joints, and the failure of symptoms to respond to salicylates eliminate the possibility of rheumatic fever. The absence of an enlarged liver and spleen and of general adenopathy does not rule out Still's disease, since these findings are frequently absent in the juvenile type of rheumatoid arthritis.

The therapy in this case should consist of continued rest, physiotherapy, gold therapy, and, if feasible, transfer of this patient to a warm, dry climate. Several blood transfusions would also be in order.

What are the prevalent forms of febrile arthritis, and how can they be differentiated one from the other? Perhaps the most prevalent types of febrile arthritis are rheumatic fever and subacute rheumatoid arthritis.

Rheumatic fever, when it occurs in its typical form, is easily recognized. It must be remembered, however, that while we think of rheumatic fever as a disease of childhood, it is quite common in young adults and occurs not infrequently in the middle decades. In the case of rheumatic fever we expect the history of a preceding respiratory infection in 60 to 75 per cent of the cases. If cultures have been taken, the infection will prove to be of Group A hemolytic streptococcal origin. Following the acute respiratory infection, which at times may be so mild as to escape detection, there is an asymptomatic period of two to three weeks; then comes the rheumatic fever, usually with an acute onset characterized by chills or chilly sensations, fever of 102 to 104 degrees, rapid pulse, profuse perspiration, prostration, and migratory pain and swelling of the joints. The joints tend to be symmetrically affected, but new joints are involved in rapid succession. The affected joints show the usual signs of inflammation, which are pain, redness, swelling, heat, and tenderness. There may be a certain amount of effusion into the joint cavity. When the affected joint is aspirated, the fluid is slightly turgid, containing twenty to thirty thousand cells per cubic millimeter.

Cardiac involvement occurs in a majority of juvenile cases and in a great percentage of all adult cases. Cardiac lesions may be endocardial, pericardial, or myocardial. Electrocardiograms, particularly if repeated every two to three days, show transitory or permanent abnormalities in more than 95 per cent of patients. The leukocyte count is elevated, there is acceleration of the sedimentation rate and, perhaps most important of all, the patient develops a relatively high titer of both antistreptolysin and antifibrinolysin in his blood serum.



RUSSELL L. CECIL

Finally, and of much importance in diagnosis, adequate administration of salicylates brings about a rapid disappearance of symptoms.

IN contrast to this picture, let us take an early case of rheumatoid arthritis in which the onset may follow an acute respiratory infection and in which the migratory character of the joint symptoms may closely simulate rheumatic fever. If, as may well be, the joints are swollen and warm to the touch and the patient's temperature is running between 101 and 102 degrees, the practitioner may well wonder which one of these two prevalent joint conditions is present. A moderate leukocytosis and elevated sedimentation rate confuse the picture still further. In a rheumatoid arthritis case, however, the heart will be negative both on physical examination and in electrocardiograms. The antistreptolysins and antifibrinolysins will be absent from the patient's serum,

and most important of all, salicylates will fail to bring about a prompt remission of symptoms. Furthermore, in rheumatoid arthritis 75 per cent of the patients develop a positive agglutination against the Group A hemolytic streptococci, but unfortunately these antibodies rarely develop before the sixth month of the disease. They therefore have comparatively little value in the differential diagnosis of acute or subacute cases.

From this description the differential diagnosis of these two conditions would appear comparatively simple. However, there are intermediate types which cause diagnostic confusion. I am thinking now of (1) rheumatic fever that progresses into a chronic joint condition indistinguishable from rheumatoid arthritis; and (2) a subacute form of secondary infectious polyarthritis which, while resembling rheumatic fever, appears to belong neither to the rheumatic fever group nor to the rheumatoid arthritis group.

So-called chronic rheumatic fever possesses all the characteristics of the juvenile disease, but fails to yield to salicylates and gradually progresses into a chronic deforming arthritis combined with chronic rheumatic heart disease. Boots claims, however, that this unusual form of rheumatic fever can be cured with massive doses of salicylates.

Subacute infectious polyarthritis has been very prevalent in the Army and Navy training camps. These patients run a subacute febrile course, have no heart lesions, and fail to respond to salicylates. However, they usually make a spontaneous recovery after running a course of several weeks or months. Boots and Dawson consider this form of arthritis as an atypical variety of rheumatic fever because some of the patients having this form show antistreptolysin in their blood serums. However, they do not respond to salicylates and for this reason alone I have never been able to accept the thesis that they belong in the rheumatic fever category. It seems more probable to me that they have mild forms of rheumatoid arthritis, which, instead of progressing into a chronic deforming disease, undergo

spontaneous recovery. As a matter of fact, many patients with genuine rheumatoid arthritis are subject to remissions and recurrences, until finally the disease takes on a chronic progressive form.

We cannot close the discussion of rheumatoid arthritis without mentioning the possibility of certain clinical variants of the disease which may run a febrile course. I am thinking now of (1) Felty's syndrome, with its swollen joints, fever, and an enlarged liver and spleen; (2) Reiter's syndrome, with fever and swollen joints in combination with urethritis and conjunctivitis; and (3) psoriatic arthritis, characterized by polyarthritis, fever, and psoriasis. This form, of course, is more frequently seen without fever, though I recall one or two severe cases where the patient ran a high fever for two months.

WHEN acute gouty arthritis appears in only one joint, such as the toe or ankle, the diagnosis is usually easy, but when gouty arthritis is polyarticular and associated with fever, as sometimes occurs, it is easily mistaken for some other form of arthritis. In this differentiation, however, the type of person attacked is important: in rheumatic fever one expects a child or adolescent; in rheumatoid arthritis, a slender, badly built, and rather psychoneurotic woman in her twenties or thirties; and in gout, a florid, middle-aged man, generally overweight. The acute gouty joint blows up very quickly and is hot, red, and extremely tender. The swelling may be quite brawny and extends some distance beyond the margins of the joint edges, giving rise occasionally to an appearance of acute cellulitis. As the process subsides, the skin may itch and desquamate. Remember, too, that acute gouty arthritis disappears almost as quickly as it comes, with complete absence of joint symptoms between attacks. The differential points for gouty arthritis are family history of gout, the finding of tophi in the helix of the ear, desquamation of the skin over the affected joints, and dramatic response to colchicine therapy. In acute gouty

arthritis the blood uric acid will be elevated in about 50 per cent of the cases.

Gonorrheal arthritis is usually polyarticular at the onset, but tends to become monoarticular eventually, and at this stage might easily be confused with gout. In the polyarticular stage with fever, it is very easy to confuse this disease with either acute rheumatoid arthritis or rheumatic fever, especially when it occurs in a young person. However, in gonorrheal arthritis the history of some genito-urinary infection can usually be obtained, the gonococcus complement fixation test is positive in more than 85 per cent of cases, and the joint fluid will yield gonococcus if cultivated on the proper medium.

It is important to recall that about half of the patients with undulant fever have polyarthritis with swelling, involving chiefly the shoulders, hips, and knees. The differentiation from other forms of subacute febrile arthritis would depend on the history of an exposure to an infection and demonstration of agglutinins and opsonins in the blood serum for *Brucella*.

IN CONCLUSION, I wish to emphasize that the physician must not forget that many other infectious diseases are complicated by arthritis. The preceding history and evidence of a specific infection are therefore essential in determining the etiology of a secondary arthritis. For example, in suppurative arthritis,

which is febrile and sometimes polyarticular, the causative micro-organism would be demonstrable in the aspirated synovial fluid. A subacute low-grade polyarthritis, with little if any demonstrable effusion, is a not infrequent complication of bacillary dysentery. Luetic arthritis, particularly that form associated with secondary lues, might possibly be confused with infectious arthritis. Careful examination, however, usually reveals other signs of syphilis. Tuberculous arthritis is nearly always monoarticular and is not likely to cause confusion for long.

So far I have made no reference to x-ray diagnosis in the various forms of subacute febrile arthritis. As might be expected, x-rays play a comparatively unimportant part in this syndrome. The reason, of course, is that in subacute arthritis a sufficient amount of time has not elapsed to permit of characteristic bony changes. The one exception would be subacute gouty arthritis in a patient who has had repeated attacks. In such cases the characteristic punched-out areas in the bone adjacent to the affected joint may or may not be demonstrable. If present, they would have considerable diagnostic value, though similar punched-out areas are sometimes seen in rheumatoid arthritis and in sarcoidosis. Hydrops of the joint may occur in almost any form of subacute arthritis and is demonstrable both by physical and x-ray examination. Unfortunately there is nothing specific about hydrops unless the fluid is found to contain pathogenic bacteria.

DIAGNOSTIC CLINIC

Biliary Disease

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THE problem of biliary disease presents difficulties that are not altogether solved.

We are indebted to Dr. Dinsmore of the Cleveland Clinic for his goodness in providing us with three cases which illustrate various phases of this disease.

The first patient is a female, forty-eight years of age who for a period of six or eight years had definite epigastric misery, characterized by intolerance to fatty foods. She gives a good textbook picture of biliary disease which culminated in 1941 with severe attacks of colicky pain requiring morphia.

The second patient has had a painless jaundice. The first patient has had no children; the second patient has had three children. Why do we stress pregnancy? The opportunity to study a large series of individuals with biliary disease, particularly those with stone, has given some varied results in regard to the relationship between child-bearing and gallstones. In a group of 83 patients of recent date, there were 12 men and 72 women; 70 of the latter were married and had had children. These data may give a distorted picture. You may find in some series

that the incidence of gallstones in women who have borne children is not so high.

Nevertheless this factor teaches a very useful lesson; namely, before accepting the diagnosis of calculous cholecystitis in an unmarried nulliparous female, one should carefully consider the patient's history and also explore all other possible diagnoses. This is necessary because during the era of "the rape of the gallbladder" when noncalculous cholecystic disease was sufficient to warrant cholecystectomy, there was indiscriminate removal of noncalculous gallbladders, with disappointing results. These disastrous results were not due to the removal of a sick gallbladder that did not have stones in it; they were due rather to operating on a patient who did not have a gallbladder disease which demanded operation. Many of those patients were suffering from psychosomatic pain; they were fatigued, they had congenital emotional instability, and their disability was often due to pylorospasm.

In that respect it is interesting to note the relationship and value of roentgenogram studies in the diagnosis of biliary disease. A study of 201 cases in the Toronto General Hospital was made by a group composed of a pathologist, radiologist, internist, and surgeon. At the end of that survey the radiologist was greatly elated because results showed that the clinical and the

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pathological diagnosis corroborated the roentgenogram diagnosis in 96 per cent of the cases. We have the highest regard for our radiological friends. They have made tremendous contributions, but the fact that the cases of calculus cholecystitis in the Toronto General Hospital correspond 96 per cent with the radiological diagnosis was not due primarily to the efficacy of our radiology department—which we think is good—but is due to the fact that the surgical staff are still clinicians and make a diagnosis based upon history, analysis, and physical examination of the patient. They don't believe that you can put the patient in a machine, turn the crank and the diagnosis will come out on the back in red ink. You still have to think and you still have to take histories and examine your patients. If you evaluate the failures of your efforts as a surgeon in treating people with biliary disease, you will find in the last analysis that the greatest number of your errors, disasters, and failures to cure are primarily the result of an error in diagnosis.

We now feel that it is worth while in the case of the nulliparous female to canvass very carefully all other causes of abdominal distress before we come to the diagnosis of gallstones. That does not mean for a moment that gallstones do not occur in nulliparous women. We have an example in a nulliparous patient here who has had recurring attacks of biliary colic for a period of five years.

That brings us to the question of why this patient has gone for five years without any operation if she has had definite biliary colic. That diagnosis was made in 1941.

We analyzed our cases repeatedly, adding the new material as it came forward. We found one fact running through all the clinical analyses, namely that a patient with biliary disease rarely got into trouble, without first receiving insistent warning in the form of biliary colic. In other words, we believe that biliary colic per se is an indication for operative therapy. We all recognize the fact that there is no therapeutic aid or procedure which is going to solve the problem in patients with calculous cholecystitis except the removal of the gallbladder and the stone.

THESE remains one group of patients with this type of disease whom operation does not cure. We canvassed our own cases until about the beginning of 1932. About that time I did a tour, and I found some of my friends telling me that they were finding many stones in the common bile duct. I kept quiet, because my experience differed. I went back and did a survey and found that we were removing stones from the common bile duct in only about 5.5 per cent of the patients upon whom we operated for calculous cholecystitis. Either I was a very bad surgeon and missing stones in the common bile duct or my friends were romancing. I knew my friends to be honest.

Therefore, starting on the first of January, 1933—and I mention the date to show you that time has proved this to be sound—we enunciated several indications for exploration of the

common bile duct in the presence of calculous cholecystitis: (1) of course, if a stone could be felt; (2) if there had been a history of jaundice, or the patient was then jaundiced; (3) if there was a dilated common bile duct; (4) if there was a thickened common bile duct; (5) if there was a thick head of the pancreas. I think we might add a sixth, to which we are not committed, and that is multiple small stones in the gallbladder with an enlarged cystic duct.

I was humiliated to find that in the first year following this procedure I was removing stones from the common bile duct in 18 per cent of the cases. Therefore, the realization that many of our failures to cure and completely relieve the symptoms of calculous cholecystitis were due to failure to remove stones from the common bile duct comes with terrific impact. In the last ten years—I have just completed the survey—we have opened the common bile duct in 42.3 per cent of all cases of calculous cholecystitis we have operated upon, and we have found stones in 22.3 per cent of the cases. That has cut down the failures in the treatment of calculous cholecystic disease to a very large extent. Nevertheless, even with that, there is still a group that does not gain complete relief.

You realize that the cause of the symptoms in calculous disease, apart from the biliary colic, has to do with a hair-trigger mechanism through the sympathetic neuro-muscular mechanism which causes great pylorospasm. As a result of this grooved pathway, after you have removed the gallbladder, your patient still has a hair-trigger pylorus. Nearly all of these patients have had previous constipation; they have been sick a long time, and they view the world through a jaundiced eye which creates a feeling of depression. Therefore, you must supervise your patients' convalescence. The physician must give the patient great reassurance and support to his mental and moral perineum; you must give some sedatives to keep him on an even keel and a little belladonna to slow down the pylorospasm.

If you will carry your patients for a period of six months after they have had their cal-

culous biliary disease operated upon, you will then end up with a group of patients who have a minimum of residual disability. That minimum of residual disability will be due to the length of time which has elapsed from the initiation of the colic to operation. This brings me back to the statement I made in the beginning—that repeated and definite biliary colic is not only an indication for operation, it is a red flag of danger.

In the group with biliary colic we find by and large about 12.5 per cent with acute cholecystitis. We find 23 per cent with stones in the common bile duct. If you are going to open the common bile duct in over 40 per cent of cases and find stones in only a little over 20 per cent, you are opening the common bile duct uselessly 50 per cent of the time. Therefore, you must satisfy yourself whether you are doing harm.

WE TOOK a group of 166 patients with stones in the common bile duct and found a 6 per cent mortality. There were 10 deaths in 166 cases. You say that is too high. Of course it is too high, but don't blame the surgeon; he did the best he could with the material available. The patients had cholangitis, they had biliary cirrhosis, they had pancreatitis, they had damaged common bile ducts, or they had damaged mucosa of the common bile ducts. The surgeon cannot put in new inner workings. The mortality is caused by associated lesions which are the result of prolonged disease.

We took another group of 246 consecutive cases of biliary disease just as they came, and we found in this over-all group that we had four deaths, a mortality of 1.6 per cent. Upon analysis of those four deaths we found that three of them fell in the common duct group. Thus there were 243 cases of uncomplicated calculous cholecystitis with one death. This is a little over a quarter of one per cent, which is the least mortality you can expect with any major surgical procedure.

WHEN you have a patient with indigestion you must make the diagnosis of biliary disease by carefully analyzing the history and making a complete physical examination. You must determine whether it is associated with colic. Do not accept just an x-ray report of a malfunctioning gallbladder. Often the story of the distress and the physical examination do not support the x-ray diagnosis. Many times we have had a patient come to us with an x-ray report of a malfunctioning gallbladder and have found that they took the dye in a village or town thirty or forty miles distant, then drove thirty or forty miles and jiggled all the dye out of the gallbladder on the way. The roentgenologist said they had a malfunctioning gallbladder. Don't blame the x-ray; blame yourself. We must have a constant technique; without a constant technique, the value of the x-rays and studies is impaired.

The next patient, forty-four years of age, had a painless jaundice which came on very suddenly with no major colics and no previous indigestion. Immediately one wonders what is happening.

In contradistinction we have a third patient who had an episode in May of this year which one could put down to structural disease. Following a meal which was rather large she had a post-meal misery, but not a definite colic, that lasted for several hours. Then she had a period of remission in which she was well until about the fifteenth of August, when, after a heavy meal, she suffered a terrifically severe pain in her abdomen, though not bad enough to require a hypodermic. Three days later she developed a severe jaundice.

With respect to this question of jaundice we so often have our undergraduate group confused and saying, "Is this an obstructive jaundice? Is this a toxic jaundice? Is it a hepatic jaundice?" How are you going to find out? The first thing they say is, "We must do a van den Bergh." If you are out in Podunk and have no laboratory, how are you going to tell whether you have a hemolytic, obstructive, or toxic jaundice? Particularly how can you differentiate a hemolytic from an obstructive

jaundice? All you have to do is look at the stool and urine. If the stool is clay-colored and the urine dark-colored, an obstructive jaundice is indicated. This tells you a lot more than the van den Bergh does. The van den Bergh is only a relative finding, as are a lot of these other icteric indices.

It is very interesting to find that both of these patients with jaundice have had children. We had an example of a painless jaundice in a boy who came in with an ulcer on his leg. He had had three skin grafts and then received a pedicle graft in an unsuccessful effort to heal the ulcer. The ulcer would not heal. The skin graft sloughed. The second skin graft sloughed. The pedicle graft sloughed. When you looked at the boy, you saw that he was mildly jaundiced, but that had not been recognized because it was rather subtle. He had never had a physical examination. May I plead that we must still be doctors despite this terrific aid in the way of physical means to the assessment of disease processes. There is no substitute for being a good doctor, listening to the patient and carrying out a complete physical examination. If you just sit down and don't talk but let the patient talk, it is amazing what useful information will come out.

Then you should examine the patient. When you examined this boy you didn't need to be clever at all because he had a spleen that came down to his umbilicus. But do not think that just because he has a spleen that comes down to his umbilicus he cannot also have something wrong in the biliary apparatus.

My introduction to surgery as a junior house surgeon came many years ago when Cammidge found peculiar crystals in the urine that were supposedly diagnostic of pancreatitis. A girl of sixteen came in with perfectly typical biliary colic. I was an enthusiast. I found Cammidge's crystals in the urine and drove my chief crazy until he would operate on this patient. I asked him to anastomose the gallbladder to the duodenum. He did it, not graciously, but to get rid of me, and when he had put in the first row of sutures and opened the gallbladder, out ran three small black stones. In high dudgeon

he stamped out of the operating room and left me in charge. I didn't know what to do. I had heard that you put a tube in the gallbladder, but I didn't know you tied it in. I put the tube in in the morning and it came out in the afternoon. Then we were in a little trouble, but I followed that girl's case for sixteen years before I could take out her spleen, and she is still well.

In the people upon whom we have done splenectomies for hemolytic icterus there have been about 80 per cent coincidental gallstones. Making a diagnosis of gallstones doesn't make it unnecessary to examine the spleen.

The question of the preoperative preparation of the jaundiced patient is so well known to you that we do not need to belabor it, but I should like to urge in this whole matter that you take a history and that you examine the patient. I urge you to accept the proposition that biliary disease with colic demands operation. If you will accept colic as the *sine qua non* for operation, you will avoid the complications of common duct infection and stone, pancreatitis, biliary cirrhosis, and all the things that go with it. In our own group we have a mortality of 6 per cent when we are dealing with the large group of common duct cases, whereas the mortality is only 0.4 per cent when we are dealing with the disease while it is still limited to the gallbladder.

If, when you operate on these patients, you will carry them afterwards for a period of six months with a little belladonna to get rid of the pylorospasm, a well-regulated life to control the constipation, and a little assurance that they are ultimately going to get well when they have routed this disturbance, you will be rewarded with a high percentage of complete cures.

The third patient here who has jaundice has gone on to a pancreatitis, and her bile has been sidetracked by a cholecystojejunostomy. This patient has had her gallbladder excised with the stones removed from the common duct. The second and third patients will take longer to get well than the first patient whose disease was limited to the gallbladder, because their disease had gone farther afield. They are not to blame; nobody is. These two represent the unusual group in which the onset is insidious. I ask you to examine your patient and to remember that jaundice may not necessarily be due to primary biliary disease. I should also like to emphasize that if a patient has chills and fever and you can exclude undulant fever and exclude pyelitis, there is most likely a stone in the common bile duct, even though the patient hasn't jaundice, because 17 per cent of the patients from whom we have removed common bile duct stones never had jaundice.

DIAGNOSTIC CLINIC

Treatment of Congestive Heart Failure

A. CARLTON ERNSTENE

THE CLEVELAND CLINIC

CONGESTIVE heart failure is a very common and important problem, and the results of strict management frequently are most gratifying.

The first case I wish to discuss is that of a white married woman, thirty-three years of age, who has no history of rheumatic fever or of its equivalents. She was admitted to the hospital on October 1, 1946, because of dyspnea upon any activity, a persistent, unproductive cough, abdominal distention, and edema of the lower legs. When she was sixteen years old, it was found that she had a heart murmur. Approximately six months ago she experienced the onset of dyspnea, followed shortly by the other symptoms enumerated.

Because of progression of the symptoms, she spent the month of July in bed and was partially digitalized. Her condition improved considerably, the dyspnea disappearing and the edema clearing. Unfortunately, however, all symptoms returned rather promptly after she was allowed up and about and they increased in severity until the time of her admission to the hospital.

Physical examination revealed moderate orthopnea, a distinct malar flush, and congestion of the jugular veins even with the patient

well propped up in bed. The heart was considerably enlarged to the left, and a diastolic thrill could be felt at the apex. On auscultation the cardiac rhythm was regular and the mitral first sound and pulmonary second sound were accentuated. Over the apex a loud, rumbling, diastolic murmur was present. There were numerous medium-moist rales over the base of both lungs; the liver extended four finger-breadths below the costal margin and was tender; and there was moderate edema of the lower legs and over the lower back.

A diagnosis of rheumatic heart disease with enlargement of the heart, mitral stenosis, and congestive heart failure was made.

X-ray examination of the chest showed the heart to be considerably enlarged, the transverse diameter measuring 15.4 cm. and the internal diameter of the chest 26 cm. There was straightening of the left border of the heart, with prominence of the pulmonary artery, and in the right anterior oblique view with barium in the esophagus, rather marked enlargement of the left auricle was demonstrated. The vascular lung markings were increased in both lungs.

The electrocardiogram showed sinus rhythm with a rate of 94 per minute. Marked right axis deviation was present, the RS-T segments

NOTE: Presented before the meeting of the Interstate Post-graduate Medical Association of North America, Cleveland, Ohio, October 15 to 18, 1946.

were depressed in leads 2 and 3, and the T waves were inverted in the same leads.

The patient was placed at rest in bed in an elevated position. Mercupurin, 2 cc., was administered intravenously promptly after her admission to the hospital. Digitalis was prescribed in doses of 0.1 gm. three times a day for four days, after which the dose was reduced to 0.1 gm. once daily for six days of each week. A low salt, acid ash diet was prescribed and no limitation was placed on the intake of fluids.

On these measures the patient has shown very satisfactory improvement. The dyspnea, orthopnea, signs of pulmonary congestion, and the edema have disappeared. There was no need for repeating the mercupurin after the initial administration.

The plan for further treatment includes a total period of six weeks of rest in bed. Digitalis will be administered indefinitely in maintenance amounts, 0.1 gm. daily for six days of each week, and the low salt diet will be continued. After completion of the period of rest in bed, the patient will be allowed up for short and gradually increasing lengths of time daily and will, of course, be kept upon a schedule of reasonably limited activity at all times in the future.

THE MOST important measures in treating congestive heart failure consist of an adequate period of rest in bed, the proper use of digitalis, the use of a low sodium diet, the administration of diuretic drugs and sedatives, the mechanical removal of fluids from the serous cavities of the body, and venesection.

Rest is an essential part of the treatment. The emphasis placed recently upon certain harmful effects of complete recumbency in the patient with advanced congestive failure does not in any way diminish the importance of a schedule of prolonged rest for every patient who has myocardial decompensation. For those patients who have failure of more than slight degree, the period of rest in bed should be at least six weeks in duration, and longer if the



A. CARLTON ERNSTENE

general condition of the patient indicates the need for it.

However, it is important to bear in mind, as Levine has pointed out, that sudden institution of strict recumbency in an individual who has advanced congestive failure may have certain deleterious effects. In congestive heart failure the venous pressure is increased approximately in proportion to the severity of the failure. This pooling of the blood in the venous side of the circulation, through direct and indirect effects, results in the appearance of edema. The edema fluid accumulates first in the dependent portions of the body and, as long as the patient is up and about, is confined principally to the lower extremities. Up to a certain point, a patient may show quite extensive edema of the legs and still present very little evidence of passive congestion in the lungs.

The enforcement of recumbency, however, may bring about a striking redistribution of the edema fluid with prompt diminution in

the edema of the legs accompanied by the appearance of edema over the lower back and an increase in the number of rales in the lungs. Also, because of the increase in pulmonary congestion, the patient's dyspnea may become more severe soon after the enforcement of the strict rest schedule.

IN PATIENTS who have advanced congestive heart failure, precautions should be taken to avoid this harmful effect of redistribution of the edema fluid. A very simple measure, recommended by Levine, and which we employ frequently, consists of placing shock blocks under the headpost of the bed so that the entire body is inclined at an angle of 30 degrees or so, with the legs dependent. This position has certain very definite advantages over the customary position of simply having the headrest of the bed elevated. In some instances it appears advisable to allow the patient to sit propped up with his legs over the edge of the bed, or even to have him spend the first few days of treatment in a comfortable chair. These measures, however, are used only temporarily, and just as soon as clinical improvement has been initiated, the customary program of strict rest in bed is proceeded with.

Congestive heart failure is the most important single indication for the use of digitalis. This is true whether the cardiac rhythm is regular or irregular because of auricular fibrillation, auricular flutter, or premature beats. When congestive heart failure is present, there are no contraindications to the administration of digitalis except for the very rare case of high-grade heart block, where the drug may induce Adams-Stokes' attacks, and the also rare situation in which the patient has a true hypersensitivity to digitalis.

Digitalization remains the only satisfactory method of dosage. This consists in the rapid or slow saturation of the patient's system with the drug until the full therapeutic effect upon the heart is secured or until toxic symptoms appear. Full therapeutic effect is judged by relief of symptoms such as dyspnea, orthopnea, cough,

malaise, and by the appearance of diuresis and an improvement in the patient's general condition. In patients who have auricular fibrillation, the ventricular rate also is a valuable guide, the aim of digitalization being to reduce the rate to approximately 70 beats per minute.

The actual schedule of dosage depends upon the urgency of the situation. In the great majority of cases of congestive heart failure, little or no urgency exists and a suitable schedule of digitalis administration consists of a dose of 0.1 gm. three times a day for a period of four days. If the situation is more urgent, this dose may be increased to 0.2 gm. three times a day for two days, or if the need for rapid digitalis action is still greater, one can give 0.3 gm. every eight hours for three doses. Even more rapid digitalization can be obtained by the oral administration of digitoxin, a preparation that is becoming increasingly popular. For the average individual a digitalizing dose of this preparation has been assumed to be 1.2 mg. given either as a single dose or in an initial dose of 0.8 mg. followed in six hours by a second dose of 0.4 mg. More extensive experience with the preparation indicates, however, that in a considerable number of individuals, doses up to 25 per cent larger than those customarily recommended may be necessary for complete digitalization.

In emergencies, and only in emergencies, one can administer digitalis intravenously. Perhaps the most suitable preparation for this purpose is ouabain. The initial dose of this drug usually is 0.5 mg. followed at intervals of four hours by additional doses of 0.1 mg. until a total of not more than 1 mg. has been given. It is important, of course, to ascertain that individuals who are to receive digitalis by intravenous injection have not received digitalis in any form during the preceding three weeks.

After the process of digitalization has been fully completed, the digitalized state should be maintained, indefinitely in most cases, by the regular administration of adequate amounts of the drug. For the average individual, a suitable maintenance amount consists of a dose of 0.1 gm. daily for five to seven days of each week.

During the past few years the importance of restricting the sodium content of the diet of the patient who has congestive heart failure has become increasingly apparent and is now generally recognized. There is still considerable difference of opinion, however, as to the optimum amount of fluid to be allowed along with the diet. At present it is our practice to employ a modification of the low salt, acid ash diet recommended by Schemm, which has a salt content of between 2 and 3 gm. per twenty-four hours. The patient is allowed to take water in whatever amounts he desires but, with rare exceptions, no attempt is made to force fluids beyond that point.

The second patient, a white woman, married, fifty-one years of age, was admitted to the hospital on September 10, 1946, because of weakness, nervousness, the loss of fourteen pounds in weight in spite of a satisfactory appetite, dyspnea on any exertion, a persistent unproductive cough, and edema of the legs. The symptoms had first appeared approximately six months earlier and had grown progressively worse.

Examination revealed that the patient was experiencing considerable respiratory distress even while at rest. A frequent unproductive cough was present. The skin was warm and moist, and there was a rather coarse digital tremor. A distinct stare and definite lid lag were present. There was a moderate-sized nodular goiter, with extension of both lobes well below the level of the clavicles. The heart was considerably enlarged to the left. Auricular fibrillation was present, with a ventricular rate of 120 beats per minute, and a moderate radial pulse deficit. A rather loud systolic murmur was present at the apex. There were numerous rales over the base of both lungs. The peripheral venous pressure was increased. The liver edge extended three finger-breadths below the costal margin and was somewhat tender, and there was moderate edema of the lower legs and over the lower back.

A diagnosis of nodular goiter with hyperthyroidism, and rheumatic-hyperthyroid heart disease with enlargement of the heart, mitral

insufficiency, auricular fibrillation and congestive heart failure, was made.

X-ray examination of the chest showed the heart to be enlarged, with straightening of the left border and prominence of the pulmonary artery. The vascular markings in both lungs were increased. The electrocardiogram showed auricular fibrillation with a ventricular rate of 124 per minute. The electrical axis was normal. The basal metabolic rate was +37 per cent and the serum cholesterol content 107 mg. per 100 cc.

The treatment instituted consisted of strict rest in bed with the patient well elevated; the administration of mercupurin, 2 cc. intravenously at the time of the patient's admission; digitalis in doses of 0.1 gm. three times a day for four days, followed by a maintenance amount of 0.1 gm. daily; a low salt, acid ash diet; Lugol's solution in doses of 10 minims three times a day; and propyl thiouracil in doses of 50 mg. three times a day.

The administration of mercupurin resulted in a satisfactory diuresis and there was prompt clinical improvement from the time of admission. The ventricular rate has been reduced to an average of 84 beats per minute, and the basal metabolic rate has dropped to +11 per cent. It was not necessary to repeat the administration of mercupurin after the initial injection.

The program of further treatment will consist of four more weeks of rest in bed, plus retention of the low salt, acid ash diet, maintenance amounts of digitalis, and continuance of the Lugol's solution and propyl thiouracil. At the end of the four weeks, thyroidectomy will be done.

ORGANIC heart disease is one of the most serious complications of hyperthyroidism. Usually the cardiac condition has caused little or no trouble prior to the onset of the hyperthyroidism. With the development of thyrotoxicosis, however, the increased load on the circulatory system frequently results in the appearance of important cardiovascular symptoms

and signs. Chief among these are auricular fibrillation and congestive heart failure.

AURICULAR fibrillation occurs, either in its continuous form or in paroxysms of longer or shorter duration, in approximately 10 per cent of all individuals with hyperthyroidism. In a second group of patients of approximately the same numerical size, the arrhythmia develops for the first time as a temporary disturbance during the first two or three days following thyroidectomy. The most important predisposing factors for the development of auricular fibrillation in patients who have hyperthyroidism are the presence of organic heart disease and the age of the patient. Approximately one-half of all thyrotoxic individuals who have auricular fibrillation before operation present evidence of organic heart disease, and approximately 75 per cent are over forty-five years old. The duration of the hyperthyroidism also is a factor of some importance; those individuals in whom hyperthyroidism has been present for a long time have a higher incidence of auricular fibrillation than do those who have had symptoms for a relatively short time.

Congestive heart failure occurs in approximately 4 per cent of all patients who have thyrotoxicosis. Usually the failure is of only mild or moderate degree, but occasionally it is quite severe. The two most important factors which predispose to the development of congestive failure in patients who have thyrotoxicosis are the presence of organic heart disease and the occurrence of uncontrolled auricular

fibrillation. Auricular fibrillation is present in approximately two-thirds of all patients who develop congestive failure, and the great majority of these either present evidence of organic heart disease or are of such an age that the possibility of degenerative changes in the myocardium cannot be excluded. Once in a while, however, failure of slight or moderate degree appears to be the direct result of uncontrolled auricular fibrillation in a young person who presents no evidence of organic heart disease. On the other hand, when congestive heart failure develops in an individual who has regular rhythm and thyrotoxicosis, evidence of organic heart disease almost invariably is present.

The treatment of thyrotoxicosis with congestive heart failure is divided into two parts; first, the management of the congestive failure along the lines already discussed, and, secondly, the treatment of the hyperthyroidism. In patients who have nodular goiters, surgery is still the definitive treatment. The duration of the pre-operative period, however, has been lengthened considerably as compared to our former practice. Now the usual patient with thyrotoxicosis and congestive failure is treated with medical measures, including the use of propyl thiouracil, for at least one month and in the majority of cases for two months before operation is carried out. In this way it is usually possible to operate upon the patient at a time when all symptoms and signs of hyperthyroidism have been controlled and the postoperative course can reasonably be expected to be entirely without incident.

During the past few years the importance of restricting the sodium content of the diet of the patient who has congestive heart failure has become increasingly apparent and is now generally recognized. There is still considerable difference of opinion, however, as to the optimum amount of fluid to be allowed along with the diet. At present it is our practice to employ a modification of the low salt, acid ash diet recommended by Schemm, which has a salt content of between 2 and 3 gm. per twenty-four hours. The patient is allowed to take water in whatever amounts he desires but, with rare exceptions, no attempt is made to force fluids beyond that point.

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the young doctor making his way than by the well-established man, who might nevertheless want to attend the course. A custom of voluntary examination for credit might meet the need of the younger man without putting any added burden on busy doctors who might attend purely out of interest or for the sake of keeping abreast of current medical progress.

L. C.

NEW ANTIBIOTICS

THE FIELD of antibiotics is now receiving major attention in modern medical research. Apparently, its potentialities have been but barely realized. Atkinson and her associates are now carrying out a survey of the native flora of Australia, in an effort to uncover important antibiotic agents.

This study, reported in *Nature*, December, 1946, is of more than ordinary interest because much of the flora of Australia, like its fauna, is unique. About 1,100 species have been examined to date, of which fifty showed antibacterial activity toward *Staphylococcus aureus*. Of these, four also affected *Bacterium typhosum*. These four species are being subjected to extensive tests. Two other species also are being given thorough study, because they were found to have anti-bacterial activity against *Mycobacterium phlei*, an acid-fast form of the same genus as the tuberculosis organism.

Here in the United States, Waksman has recently reported a new antibiotic, which he believes can be used in conjunction with streptomycin. One of the big problems of streptomycin therapy is the development of bacterial resistance to the drug. Waksman points out that the new antibiotic, when combined with streptomycin, will eliminate bacterial resistance. If clinical results show this to be the case, it is indeed an important discovery, for streptomycin has been found most useful in combatting organisms that cause chronic diseases. Hence, the drug must be given over long periods of time. Bacterial resistance is the frequent and disappointing consequence.

CHLOROPHYLL THERAPY

THE traditional description of a chemotherapeutic agent is one that destroys the invading organisms without damaging the tissues of the host. Occasionally, the obverse approach is found desirable. That is, the host tissues are stimulated to greater defensive activity, or are so altered in character that they can repel bacterial invasion. Thus, estrogens have been found valuable in the treatment of gonorrheal vaginitis in children. The drug acts as a stimulant to the growth of the epithelial cells that line the female reproductive tract. Similarly, chlorophyll has been shown to affect favorably the course of wound-healing by host cell stimulation.

In the *American Journal of Surgery*, January, 1947, Bowers has reviewed the literature on the chlorophyll therapy of wounds and has reported additional experiences with this compound at an army general hospital. One hundred and one surgical patients were treated, suffering from pilonidal cyst wounds, fistula-in-ano, ulcerative colitis, thoracic empyema, gunshot wounds, burns, decubitus ulcer, and various other conditions. The chlorophyll was applied as a wet dressing, ointment, or by irrigation. Another 119 orthopedic cases—compound fractures—were treated, as well as 132 EENT patients and 10 patients with urological conditions. The data regarding treatment were reported by thirty-five different medical officers, over a period of nine months.

The officers were impressed with the rapid disappearance of objectionable odors and the remarkable cleanliness of the wounds within two or three days. Fine textured and firm granulation tissue formed readily; epithelization was stimulated more than with other agents. The dressings were most comfortable to patients, and did not cause toxic reactions. In suppurating cases, the chlorophyll caused cessation of pus formation in two or three days. Chlorophyll instillations of the nose and sinuses caused rapid changes in the nasal mucosa, with prompt relief from purulent discharge, freer breathing, and without disagreeable after effects.

Bowers does not claim chlorophyll to be antibacterial. Its benefit is derived from its ability to stimulate the host cells. As proof of its efficacy, Bowers mentions that his hospital uses only one-third to one-half as much penicillin as is used by other army hospitals treating similar cases.

R. W. C.

CREATIVE MEDICINE IN A SMALL TOWN

ONCE upon a time there was a young doctor who decided to go into the public health field, thinking that in it he could serve the greatest number of people in the most effective way. Qualifying himself thoroughly, with graduate training and a certificate, he won a position as county health officer in a midwestern state. But though successful as health officers go, he did not get the satisfaction he hoped for from his work. Over and over again he found himself telling people what up-to-date medicine could do for them; but again and again it happened that the services they needed were unavailable in the community. The situation was a general one—he did not blame anybody for it—nevertheless there it was.

He decided that he would himself try to bring people the services he had been recommending. Gaining the consent and cheerful cooperation of his family, he gave up his comfortable job in a pleasant town and moved to a poor community with no advantages for living or practice beyond the existence of a large number of people without proper medical care. Obstetrics, he thought, offered an entering wedge for what he meant to do. He saw it as the doorway to a vista stretching into the future; he could already see pediatrics and school work following naturally in their turn.

So it turned out. He took his obstetrics as seriously as he did everything else, ready for

any emergency he could foresee, knowing that there was an absolute dependence upon him. He brought babies into the world and became advisor to their mothers. Care of the babies and care of the other children was the next step; then his public health training made the school work almost inevitable.

In fitting up his office he bore his ideal in mind. Into it went every diagnostic aid he could use: good general examination equipment, ophthalmoscope, x-ray, and a laboratory. Finding a bright young high school graduate who was unable to go away to school he trained her himself as his laboratory technician. In the laboratory were an electrocardiograph, a photoelectric cell for color determinations, and other less common equipment. Besides his regular obstetric and pediatric work his ideal included emergency service to the community in acute cases, either medical or surgical. However, in the normal course of things he refers all his surgery and the more complicated medical cases.

As his practice grew he developed a small hospital, for obstetric and emergency cases only. The community began to realize that here was a man. Remembering how he had come to them and seeing the inestimable worth of what he had created, they turned out one day 1500 strong to honor him at a reception. He is no saint or prodigy but a normal man, an honest doctor blessed with purpose and a good personality, with a simple belief in proper diagnosis and treatment, and a knowledge of his own limitations. He has earned every bit of the gratitude and affection that have been poured upon him.

This is not a fairy tale. It is a case described in a recent Bulletin of the Minnesota State Medical Society. It is a fair description of the need that is today so real and pressing for the kind of service that a general practitioner can render, and of the kind of reward he can fairly hope to win.

R. O.

This Month in Medicine

INJUDICIOUS ENDOCRINE THERAPY

THE indiscriminate use of endocrine compounds in the control of abnormal uterine bleeding might mask the underlying organic cause. Some two years ago Scheffey and his associates reported a series of cases of uterine cancer in which the correct diagnosis was delayed because of the injudicious use of endocrine preparations. These investigators emphasized the possible dangers and diagnostic confusion that result from such practices.

Recently, Pollack and Taylor have reported a case in point, in which the patient took stilbestrol for the purpose of controlling uterine bleeding. The patient, an 18-year-old woman, had refused dilatation and curettage because of her virginity. The stilbestrol was administered for two years or more, until finally the discharge and bleeding became so foul and profuse that curettage and dilatation were permitted. The diagnosis was adenocarcinoma, grade III.

This patient was young, so young that uterine carcinoma would hardly have been suspected. However, Pollack and Taylor point out that carcinoma during the first two decades of life is not so rare as has been supposed. They review the data from the literature, regarding 30 such patients. In 22 of these patients the diagnosis was adenocarcinoma. The prognosis is grave; only four patients survived five years. Early and accurate diagnosis, therefore, is mandatory. Any palliative therapy which masks the true state of affairs, which gives the physician and patient a sense of security in the face of potentially impending danger, is ill-advised.

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CIRCUMCISION AND VENEREAL DISEASE

SINCE time immemorial, the value of routine circumcision has been a subject of medical, religious, and lay controversy. Seldom, however, have sound data regarding the virtues of this practice been marshalled. Wilson presents an interesting factual study of this problem. At a Canadian Army V.D. treatment center, 1,304 consecutive patients were investigated to determine their final diagnosis and whether previously, they had been circumcised. Of these 1,304 patients, 76.7 per cent had not been. A control group of 1,000 Canadian Army recruits was examined to determine the incidence of circumcision in Canadian Army personnel. Of the 1,000 controls, 52 per cent had been circumcised men. The author concludes that "the presence of a foreskin is a distinct liability to the average soldier."

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THIOURACIL IN THYROTOXICOSIS

PERSISTENT post-therapeutic remission may be expected in a large percentage of thyrotoxic patients who are treated with thiouracil. A few months ago Beierwaltes and Sturgis reported their results in the thiouracil treatment of 45 patients with toxic hyperplastic goiter. A total of 29 patients were followed for over four months after treatment. When the drug was administered for as much as ten months, 60 to 80 per cent of the patients remained in remission during the period of observation, that is, up to twelve months after discontinuing the thiouracil. The authors conclude, therefore, that for selected cases of thyrotoxicosis, thiouracil treatment may ultimately prove as satisfactory as thyroidectomy.

Recently, Rose and McConnell have confirmed these findings. They treated with thiouracil 35 thyrotoxic patients, for periods of one to nineteen months, after which they were under observation for seven to thirty months. Of their series, 45.7 per cent have remained in remission three to twenty-nine months after drug withdrawal, and 25.7 per cent have remained in remission for a year or more. These patients with sustained remissions had suffered from uncomplicated thyrotoxicosis of mild or moderate severity. Four patients relapsed upon withdrawal of treatment, but following another course of treatment they showed a sustained remission. Six patients did not respond to prolonged treatment; they were in the older age groups and were suffering from complicating diseases.

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Rose, E., and McConnell, J.: Thiouracil in thyrotoxicosis. Results of prolonged treatment in 35 cases. *A. J. Med. Sci.*, 213:74, January, 1947.

HUMAN GLANDERS

HUMAN glanders is a rare disease in this country, although in other parts of the world, where veterinary control measures are lax, it has been observed rather frequently. Here, laboratory infections are the more common. Some authorities, however, affirm that it probably is more frequent than supposed, but that it is usually mistaken for some other disease. When it does strike, the prognosis is grave. The acute disease is of rapid onset. It may appear as a bronchopneumonia or lobar pneumonia, with or without bacteremia. Or it may be a generalized pyemia. The disease is usually fatal in ten to thirty days; in the severe acute form, mortality approaches 100 per cent.

In view of the serious outcome of glanders infections, the work of Howe and Miller is of interest. These investigators point out that all treatments mentioned in the literature have been found ineffectual. They were unable to find reports of investigations in which the sulfonamides or antibiotics were tried. However, the disease in experimental animals was known to yield to sulfadiazine. Consequently, when confronted with six cases of gland-

ers among laboratory personnel, they administered sulfadiazine. In general, their patients appeared to respond well to treatment, although two of them were improving when the chemotherapy was begun. Two patients responded dramatically; one experienced a sharp drop in temperature within forty-eight hours after the sulfadiazine was first administered.

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SLEEP AND HYPNOTIC TRANCE

WHAT is sleep? Is it similar or related to the hypnotic trance? Some investigators have claimed that the two phenomena are entirely different, while others have held that hypnosis is a sleep variant, a "sleep-like state," or an "artificial sleep." Until the electroencephalograph was discovered, the question had no adequate answer. A recently reported encephalographic study, however, has produced objective data that are of interest.

Dynes, of the Lahey Clinic, made electroencephalograms of five patients while in the waking state and in hypnotic trance. The leads to the electroencephalograph were taken from the frontal, parietal, and occipital regions. All of the patients were capable of being placed in a deep hypnotic trance. In general, the electroencephalograms taken during the waking state are not significantly different from those obtained during hypnotic trance. One patient had been so conditioned that he would pass into a trance almost instantaneously. Recordings were made of this individual, while the transition was taking place. Apparently, cortical electric activity was not altered in the least by his passage from the waking into the hypnotic state. Dynes concludes, therefore, that the hypnotic and waking states are more or less identical electroencephalographically.

Sleep is different. The recordings are entirely unlike those obtained from a person who is awake or in a trance. Hence, this objective evidence suggests that hypnosis is not a sleep variant.

SUGGESTED READING

Dynes, J. B.: Objective method for distinguishing sleep from the hypnotic trance. *Arch. Neuro. & Psychiat.*, 57:84, January, 1947.
R. W. C.

Consultation Service

We offer this special consultation information service as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from members of our editorial board best qualified to help. Each question will be answered by mail and answers of general interest will be published each month.

SUBDELTOID BURSITIS

QUESTION: *What is the most successful treatment of subdeltoid bursitis with calcareous deposits in the shoulder. Is the treatment different if the condition has been present one month or six months?*

M. D.—OHIO

ANSWER: Subdeltoid bursitis is a periarthritides in which the supraspinatus tendon becomes partially calcified and, presumably, following trauma some of the calcium granules are broken off into the subdeltoid bursa. Bleeding may occur into the bursa at the time of injury. It is important to point out that calcification may occur in the subacromial or subdeltoid bursa without pain being present. The finding of x-ray changes therefore need not always indicate active therapy. Moreover calcium in this location has been seen to disappear spontaneously (without any treatment) although this is unusual. Characteristically, pain occurs in the tip of the shoulder and radiates to the deltoid insertion at the humerus. Abduction and rotation are limited because of pain.

The patient should first be instructed to move his shoulder through the maximum range of motion, attempting normal excursion at least once or twice a day, irregardless of the treatment. The shoulder joint is particularly prone to rapid capsular and periarthritic ankylosis with the resultant frozen shoulder. This is likely to occur when a

patient is afraid to move the arm because of pain and keeps it immobilized at his side.

Treatment may consist of x-ray therapy or physical medicine. Probably x-ray therapy used in the acute stage is the treatment of choice. If pain is extremely severe, procaine injection or surgical incision and drainage have been recommended. Later, needling of the bursa to produce traumatic small hemorrhages, with the injection of a small amount of saline has been used by some with success. Washing the bursa out is not recommended.

In the acute stage x-ray therapy may be given as follows:

Approximately 100 r (96 to 108r) two or three times at daily intervals. With the exception of the exercises mentioned before, the joint should be rested most of the time during the day when x-ray therapy is given. If pain is located anteriorly one large field over the anterior shoulder may be used, otherwise an anterior and a posterior field are used. Four mm. of aluminum filters, $\frac{1}{2}$ value layer of 0.24 mm. copper, 40 cm., MA 6, time $2\frac{1}{2}$ to 3 min. A second course may be given after 3 or 4 weeks. In the chronic stage, a larger dose of radium is employed, around 150 r, and at less frequent intervals (two or three times at intervals of 3 or 4 days).

Physical therapy includes the use of diathermy, massage and exercise. If the pain is localized the short wave diathermy may be used. The conventional diathermy produced by the old type of high frequency machines is, however, often preferable. With this apparatus a plate is used over the shoulder. Treatment should be given daily for 10 to 14 days, each time for approximately 40 minutes followed by 10 minutes of massage and 5 minutes of exercise. Therapeutic exercise includes attempt of normal range to the point of pain, with active assistance from the therapist. Physical therapy may be used primarily or may be used following complete or partial failure of x-ray therapy.

MEN OF MEDICINE

T. H. SOLLMANN—PHARMACOLOGIST

ALTHOUGH Dr. Torald H. Sollmann was officially retired three years ago, he goes about his work in his little laboratory in the department of pharmacology, Western Reserve University, with the spirit of a young man just starting his career. On the table is a row of fish bowls, each containing a pair of goldfish, swimming about and swishing their tails. Into one of the bowls, he pours some alcohol. His face lights up with curious amusement to see the fish listless in an alcoholic stupor. It is part of his experiments on drug action.

Dr. Sollmann served as head of the department of pharmacology and dean of the Western Reserve School of Medicine until his retirement in 1944. He has produced more than 500 scientific papers on the subject of pharmacology. He has taught a host of scientists, many of whom are gray-haired and honored internationally for their work. But "Solly" is a pioneer—a searcher. To him, the great reservoir of the unknown is still a new frontier.

Accustomed to long hours of work, he is still seeking the answer to a key problem in medicine—why certain drugs act the way they do on living creatures. Or more particularly—what is the correlation between the action of drugs and their chemical structures?

When you visit him in his laboratory, he is always ready to greet you with a smile. Frequently

brushing back his gray stubbly hair, he talks with a husky voice and a slight German accent. Behind his quiet, gentle manner is an interior of tough fiber.

"Solly" is happiest when he has an extra-difficult problem to solve. He likes to match wits with the unknown. He developed this characteristic as a boy in Coburg, Germany, where he was born 73 years ago. For his father, a botanist and mycologist of distinction, was an exacting teacher.

He would take his son on long and strenuous walks through the woods—in all seasons of the year. The winter, however, was the time to teach the boy about trees and how to identify them. "Any goose can recognize a tree with leaves on it," the botanist said. And today "Solly" knows his trees, as well as he knows the peculiarities of hundreds of drugs. He has continued his long walks, and maintained his love of trees throughout his life. In his rare moments of leisure, he hikes with pen and ink in his pocket and pad of paper under his arm. When he finds a tree that fascinates him he sketches it. That is one of his diversions he has faithfully observed.

Since Dr. Sollmann was one of nine children, he has some doubts about birth control. "If my family had practiced it, I would not have been here," he chuckles. His parents were deeply religious and gave him a strict Lutheran upbringing.



At 13 young Sollmann came to Canton, Ohio, to live with his brother Luitpold. The smell of the drugs, the mystery of their action, fired his imagination. He wanted to learn more about them, as much as he possibly could. He studied what books he could find—on how to learn to speak and write in English, books about drugs and books about medicine in general.

In four years he decided he had learned enough to permit him to pass the state board examination. He went to Cleveland and submitted to the tests. He passed them with the distinction of being the youngest person to obtain a druggist's license in Ohio, up to that time.

That was an unusual achievement, enough to satisfy any number of intelligent 17-year-olds. But young Sollmann was not satisfied. It was merely a stepping stone to something better. He set up a branch store for his brother, not merely to establish a business and settle down, but to make some money so he could go on to more ambitious ventures. In two years he had enough saved to take another important step. He left for Paris, and there he studied at the Val de Grace, a military hospital. He explored the new field of food chemistry, and the detection of adulterants.

Learning all that his Paris venture and his money permitted, he returned to Ohio, and going to Cleveland, he entered Western Reserve University as a second year student and an assistant in chemistry, histology, pathology, and physiology. There were no extra-curricular activities—no dances or other social affairs—for him. He was too fascinated with his subject. Chemistry, physiology and the rest were fun. Working at them was fun enough for this 20-year-old explorer into the unknown.

His thoughts and ideas were crystallizing—and the seed of that crystal was the action of drugs on living creatures. There was not much known about all this then, not as compared with the vast amount of knowledge that has accumulated today. Pharmacology departments in medical schools were rare. The first in America had been established at the University of Michigan, the second at Johns Hopkins, and the third at Western Reserve.

The subject was so new that there was no textbook on it in the English language.

That was the state of things when in 1896 after

graduation young Sollmann remained to teach. A year later he accepted the direction of the department of pharmacology, but there was no textbook, no laboratory manual that would help him in his teaching. That did not deter him. He wrote his own textbook: "Laboratory Experiments in Pharmacology." It was a small thin book of 100 pages. From this beginning grew his gigantic text, "Manual of Pharmacology," with 1,000 pages. It is a standard text on the subject in which he has made many sharp and critical revisions.

Dr. Sollmann's department of pharmacology at Western Reserve University became one of the most distinguished of its kind in the United States, and drew students from all parts of the country. His distinguished pupils, such as Dr. Paul Hanzlik, professor of pharmacology at Stanford University; Dr. Robert E. Hatcher, late professor emeritus at Cornell University, and Dr. Edgar Brown, formerly associate professor of pharmacology at the University of Minnesota, were fond of referring to him as the "daddy of pharmacology."

As a teacher "Solly" never had the reputation of being a fine raconteur of yarns, but he kept the students' attention by demanding close observation and exacting work.

"Solly" has been a great admirer of his late colleague at Western Reserve, Dr. G. N. Stewart, and has followed Dr. Stewart's precepts. "With modified severity," Dr. Sollmann relates, "Stewart exacted thoroughness from his students. He was a master in exposing the slipshod. With a few artistic moves he peeled off the cloak, skin, muscles and bones of his victim, and reduced him to a shadowy cloud. He did all this with such evident absence of malice that the culprit learned an unforgettable lesson without taking offense."

Dr. Sollmann, early in his career, was a strong advocate of supplementing the textbook with first hand observation. In the early days, the Western Reserve Medical School found itself with a fine new building in downtown Cleveland and an endowment of \$125,000. This huge sum for those days was too rich for the blood of some of the professors, especially the old ones. They wanted it spent on salaries. But the younger faculty men were willing



"There are at least 999 out of 1,000 chances that every disease will be conquered—except death. Perhaps the span of life can be increased to 125 years. One can never know."

Although Dr. Sollmann has several hobbies, playing the violin, making pen and ink drawings, hiking, and collecting old medical books, he says his chief recreation is work. He is sociable and can enjoy himself thoroughly at a party such as the annual gatherings of the Medical School Alumni. He married Miss Alice M. Sersell in June, 1902, and they live in a modest home in suburban Cleveland Heights. Before his retirement as dean of the School of Medicine and as head of the department of pharmacology in 1944 he was accustomed to working 80 to 100 hours a week. His work week now has been trimmed to 60 to 80 hours.

Throughout his long career Dr. Sollmann has set an example to young medical and scientific students. "Any young person wanting to be a physician must realize that a physician's life is not a glamorous one; it is a life of hard work," he has warned students scores of times. "A physician will be unhappy unless he has the right feeling toward his work. He will not have the right feeling unless he is a good physician, and to be a good physician he must love work."

"A physician must also be interested in people and have very little interest in himself. He must take as much college work as circumstances will permit, and in addition to his own specialty he must broaden himself as much as possible. This does not mean being a good fellow, for that leads to disaster."

"And finally, a physician to the end of his career, must never quit studying."

During his life of hard work as a research scientist he has formed some broad views of the aims of research and the motives behind them. He is equally tolerant of the research scientist who dares to make wild conjectures and the scientist who is so cautious that he wants to know the figure in the next decimal point. Both have their places in research, he believes.

He says research can be a good hobby, and does not have to have "all the visés of respectability on

to sacrifice salaries for adequate laboratory facilities, so the students could repeat the experiments about which they had read. The younger men won, and the laboratories were installed. This was in 1893, so when Dr. Sollmann entered the next year it was the beginning of a new era—an era of supplementing book-learning with first hand observation.

So many new developments have occurred in science and medicine since those days, that Dr. Sollmann can only contemplate them in amazement—the X-ray, radium, and all that have developed from them, such as the transmutation of the elements, radioactive isotopes; synthetic drugs, the sulfonamides, penicillin, vitamins, and hormones. Electrocardiography, electroencephalography, the complexity of anesthesiology, and other developments have taken place since his early student days. "At that time the transmutation of the elements was considered just as impossible as the perpetual motion machine," he remarks. He has seen so much happen in his time that he is filled with an almost consuming optimism as to the future of medicine.

its passport." He will take no part in the contention between fundamental and applied research, believing each of equal importance. Without fundamental research, he says, there can be no applied. And the few people who make deeply significant discoveries in fundamental research could not flourish if results of fundamental work were not applied.

Dr. Sollmann believes that a research worker must love research. To those who do not care to have a part in this sort of work, the spirit and enjoyment of it cannot be interpreted.

In his own work he has never resorted to the use of elaborate apparatus. His experiments usually entail direct application of drugs and chemicals on living organisms and organs, with observation of their reactions. He has been interested in a great many problems. "All things interest me," he says, "and there are few fields in pharmacology in which I haven't dabbled."

The teacher, Dr. Sollmann believes, should love those who are striving to learn, should love and appreciate the spirit of the learner, have a fund of patience and tact. He should be able to put himself in his student's place in order to understand him.

Dr. Sollmann was named dean of the Western Reserve School of Medicine in 1928, and during his service as dean, he insisted upon increasingly better standards of selection of students. He has insisted upon a good balance in the student between abilities as a practitioner and capacity for scientific work. Under Dr. Sollmann the school tried to develop the students' personality, emphasizing individuality. He has urged the faculty to take a great personal interest in the students.

Dr. Sollmann has played an important part in the policies adopted by the Association of American Medical colleges toward the selection of students. In the early 1920's the applicants for admission to medical schools began to outnumber in an overwhelming ratio those who could be accepted. At one of the meetings of the Association, a psychologist presented a selection test, purporting to forecast the success of students in the study of medicine.

Although he was skeptical of the test, Dr. Soll-

mann was made chairman of a committee to investigate it. He had it tried out in a number of schools. There was a good correlation between its predictions and the results. He changed his mind, and became a strong advocate of its use. He faced opposition for several years but stuck to his guns. "Some of those opposing it thought the test was not vital," he relates. "Others thought if an applicant for admission took the test and passed it, the job of turning him down if he were not wanted for other reasons would be difficult. But there was one answer—the test worked. I had to do a good deal of fighting to keep it going. Although the test in its original form has been modified, it has proved very useful."

Dr. Sollmann was one of the pioneers in his field of teaching to appreciate the value of the motion picture in the presentation of facts. He was one of the first to introduce movies in instruction in pharmacology, and has made twenty-eight different films. They include such titles as "Digitalis on Frog Heart"; "Strychnine Convulsions on Rabbit and the Control by 'Laying on Hands'"; "Morphinized and Decapitated Frogs"; "Polyneuritis—Pigeons on Rice Diet; Recovery After Addition of Vitamin B." In response to widespread demand, they have been shipped to schools in all parts of the world.

He recognized early that movies could in ten or fifteen minutes impart as much information as lectures and demonstrations could convey in hours and days.

In his career as a teacher he emphasized the value of demonstrations by the professor and instructor, to supplement experimental work. He believed that students could learn better by seeing demonstrations than they could by individual work, especially if they were well prepared in physiology or similar studies. He admits, however, that he did not succeed in having this idea generally adopted.

When he engaged a member of the faculty, Dr. Sollmann made a very searching analysis of the qualities of each man, and then when his men were selected he would not interfere with their judgment or decisions, except for an occasional suggestion.

In addition to his work at Western Reserve, Dr. Sollmann has rendered many public services. He has been chairman of the Council of Pharmacy and

Chemistry of the American Medical Association for many years, and in that position has added his knowledge, experience and judgment to help it become an enormous influence on the suppression of patent medicines and quackery, and to become an important guide to doctors in the treatment of injury and disease.

For forty years Dr. Sollmann has been an important contender in the fight for high standards of pharmaceuticals. As a member of the convention that determines the policies of the United States Pharmacopeia, Dr. Sollmann advocated thirty years ago that the scope of the articles that go into this publication should be decided by the medical members of the convention. The pharmacist members fought him, but he doggedly stood his ground for twenty years and won. His opponents took the view that if a medicinal were prescribed by any physician it should be acceptable. His viewpoint was that leading authorities in medicine should be the judges.

On the Council of Pharmacy and Chemistry he was among those who fought to have all essential ingredients in drugs listed on the labels of their containers. His perseverance and that of his colleagues resulted in the enactment of that policy into law.

During World War I he was mustard gas consultant for the United States Army and reported on many experiments in the treatment of mustard gas burns. He also has performed important service to industry and the industrial worker as a consultant in industrial poisoning.

Because the effect of alcohol and tobacco are discussed in his classic "Manual of Pharmacology" it frequently became a spirited classroom topic. But his statements on this subject are often rather inconclusive. He is tolerant of the drinker and the smoker, and is not fearful of the consequences to the race as a result of indulgence. He believes those that are harmed will be eliminated and the race will continue.

Dr. Sollmann has a broad, tolerant view of many current issues. It is hard to engage in an argument with him. On the question of medical care, for example, he agrees that every citizen should have full benefit of modern medical care. He also thinks that the means should be worked out with due deliberation. If the medical profession seems a little tardy, he says, "it may be dizziness at the swirl of things rather than apathy. It may be a professional preference to have the buts before rather than behind."

Book of the Month—A Report

POSTGRADUATE OBSTETRICS*

A SHORT but highly informative course in practical obstetrics is presented in book form by William F. Mengert, M.D., of Dallas, Texas. A large fund of factual information is concentrated into a relatively small book by minimizing historical detail, controversial discussion, and items of purely academic interest. The suggestions for managing obstetrical complications are based on generally accepted principles. Preventive measures are stressed and the physician is given the "don'ts" as well as the "do's" of treatment. The material is presented in an easily readable and well-organized fashion, by a physician who has spent the major part of his professional life in the teaching, clinical investigation, and practice of obstetrics and gynecology.

The author explains in the preface how he planned and organized his work. A given subject is allotted space roughly in proportion to the frequency of its appearance during a lifetime of experience with obstetrics by the physician in an average community. This experience is estimated to include 1800 deliveries of which 40 to 100 are forceps operations, 50 to 60 are breech extractions, and 10 to 30 are cesarean sections. Complications encountered include 10 to 20 eclampsies, 20 to 50 women with pyelitis, 70 to 90 women with minor degrees of pelvic contraction, 18 each of placenta previa and prolapsed cord and about 300 to 400 women with abortion. Two or three women will die from puerperal infection, 90 will be seriously ill and 450 will have morbid temperature eleva-

tions. About 20 sets of twins will be delivered but only one in four physicians will deliver triplets. Certain diseases of special interest or conditions that offer greater potential maternal or fetal hazard are given more space than would be indicated by their frequency of occurrence.

The contents of the book are divided into three sections dealing with pregnancy, labor, and the puerperium, respectively. The opening chapter deals with the diagnosis of pregnancy. Following this, prenatal care is discussed with particular stress placed on the prevention of toxemia, and the recognition and early treatment of syphilis. Minor ailments of pregnancy have a great nuisance value for both physician and patient. Sound principles are presented for the treatment of such annoying conditions as heartburn, hemorrhoids, varicose veins, etc.

The importance of adequate treatment of anemia before the pregnant patient reaches term is emphasized in a chapter on disease complications related to pregnancy. For the treatment of pernicious vomiting of pregnancy, a regimen is described that was used for 206 patients without need arising for a single therapeutic abortion. In his discussion of the toxemias of pregnancy, the author presents a useful summary of the conditions under which a patient with hypertensive disease may justifiably be carried to term pregnancy. Practical rules for the treatment of mild and severe preeclampsia are presented. The conservative treatment of eclampsia is followed, the convulsions being controlled with heavy doses of sedative drugs, chiefly morphine. Figures are presented to show that forcible delivery of the eclamptic patient by either vaginal or abdominal route, doubles her chance of dying.

*Postgraduate Obstetrics. By William F. Mengert, M.D. 302 pages, including index. 123 illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper and Brothers, New York, 1947. \$5.00.

A chapter on abnormal pregnancy includes the discussion of ectopic pregnancy, hydatiform mole, and chorionepithelioma. The author has found cul de sac exploration valuable for diagnosis when ectopic pregnancy is suspected. A simple method of autotransfusion is described for use when free blood is found in the peritoneal cavity at the time of laparotomy. Rapid enlargement of the uterus particularly in the lateral diameter may be a sign of hydatiform mole, especially when associated with abnormal bleeding early in pregnancy. Following the removal of the mole, pregnancy tests are used over a two-year period to help in the detection of chorionepithelioma.

For the management of the patient with antepartum hemorrhage, the author recommends immediate hospitalization, selection of a compatible donor for blood transfusion and prompt termination of pregnancy when the diagnosis of placenta previa is established. Simple measures of treatment and vaginal delivery may be used in 75 per cent of all cases of placenta previa with minimal danger to the mother and with a fetal mortality rate of less than 20 per cent. Methods described for the vaginal control of bleeding include simple rupture of membranes, scalp traction, use of the hydrostatic bag and Braxton Hick's version. The last two methods increase the fetal risk and should be avoided if possible. The author reserves abdominal delivery for complete or severe grades of placenta previa.

Dr. Mengert believes that proficiency in the determination of pelvic measurements is rarely achieved by anyone but the obstetrical specialist. Therefore he emphasizes the use of clinical tests rather than pelvimetry for the estimation of pelvic capacity. For the estimation of inlet capacity, the author describes a test for disproportion and the impression maneuver. The fist test is used for estimating outlet capacity. Midpelvic inadequacy is suspected with the history of difficult labor and findings of normal inlet and outlet capacity, prominent ischial spines, sacral deformity, and non-engagement of the fetal head at term in the primigravida.

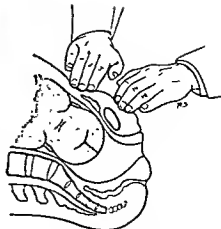
The second section of the book is devoted to labor. Following a discussion of the conduct of normal labor, a chapter is devoted to obstetric

analgesia and anesthesia. There is no ideal obstetric anesthetic agent but the best available methods are presented and carefully evaluated. The technic of pudendal block anesthesia is detailed and illustrated. The pros and cons of caudal anesthesia are discussed and the author concludes that the physician who administers caudal anesthesia must be adequately trained and prepared to be in constant attendance throughout the course of labor.

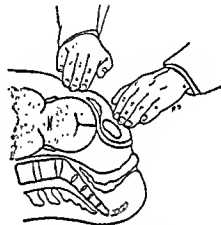
The subject of postpartum hemorrhage is given particular attention in line with its importance as a leading cause of maternal mortality. Routine prenatal blood typing and Rh factor determination are suggested for patients who are to deliver in hospitals without blood banks. Plasma is to be used only as an emergency measure, while preparations for transfusion are proceeding. The various methods for the control of hemorrhage are described, in logical sequence, ranging from simple massage and oxytocics to the use of hysterectomy in the rare instances when other methods fail. The author recommends use of a sterile intrauterine douche to stimulate uterine contraction and to wash out blood clots following manual removal of the placenta or in the event of postpartum hemorrhage.

The various types of obstetric forceps and indications for their uses are described. Failure to observe the rule that the cervix must be dilated or easily dilatable is cited as the cause of more harm in the application of forceps than any other single factor. The author describes in some detail the intrauterine rotation of the anterior blade of the Kjelland forceps in cases of transverse arrest of the fetal head.

In his discussion of cesarean section, Dr. Mengert presents figures to show that even under ideal circumstances the operation is accompanied by a maternal mortality rate that is 3 to 4 times that of normal birth and a fetal hazard that is increased at least twofold. Three rules that he feels should be "graven on the physician's mind" are (1) that the operation is not and should not be an emergency procedure; (2) the mortality rate of the operation rises sharply with every hour of labor; and (3) in the presence of infection the operation is best followed by hysterectomy. The last rule will



Disproportion test. Normal. The fetal head is in the pelvis and does not override the symphysis, as shown in the accompanying diagram.



From: "Postgraduate Obstetrics" by Mengert.

Disproportion test. Abnormal. The fetal head does not enter the pelvic inlet and overrides the symphysis, as shown in the accompanying diagram.

be disputed by those who favor the extraperitoneal type of section.

In prolonged labor, prophylactic administration of penicillin or sulfadiazine is used to prevent intrapartum infection of the amnion or the fetus or both. Operative interference is to be avoided since it doubles or triples the hazards of prolonged labor. For the management of labor in breech presentation, the author lists nine principles. He considers the most important of them to be to permit preliminary dilatation of the maternal soft parts by the fetus before interference is started.

The last section of the book is devoted to the puerperium, normal and abnormal, the care of the newborn, diseases of the newborn, follow-up examination of the mother, sterility, the emotional

stresses of pregnancy, and laboratory and ward procedures. A chapter devoted to puerperal infection is particularly helpful in relating the different types of puerperal infections to their time of onset.

"Postgraduate Obstetrics" represents the end result of what must have involved considerable detail work for the author in construction and organization. For many years Dr. Mengert served on the teaching staff of the University of Iowa Medical School under that well-known obstetrical teacher, Dr. E. D. Plass. In 1943, Dr. Mengert left Iowa to become Professor and Chairman of the Department of Obstetrics and Gynecology at Southwestern Medical College, and Parkland Hospital, Dallas, Texas. Thus the views expressed in "Postgraduate Obstetrics" represent to a considerable degree, the teaching policy of these two medical centers.

TIME RELATIONSHIPS OF PUERPERAL INFECTIONS

POSTPARTUM DAY	ONSET OF TYPES OF PUERPERAL INFECTION
2 to 5	<i>Endometritis.</i> The more vicious infections appear early. Those appearing later are generally milder but tend to produce putrid lochia. Puerperal endometritis virtually never begins after the fifth day.
3 to 4	<i>Peritonitis, septicemia, or both.</i> There is always antecedent or concomitant endometritis. Peritonitis is suggested by spreading abdominal tenderness and distention. Septicemia is suspected with all severe acute cases of endometritis.
6 or 7 and thereafter	<i>Mastitis.</i> There is seldom antecedent fever.
6 to 9	<i>Pelvic cellulitis or parametritis.</i> There is antecedent endometritis, mild or severe.
9 to 11	<i>Acute gonorrheal pelvic inflammatory disease.</i> Comparatively uncommon.
10 to 15	<i>Thrombophlebitis.</i> Generally there is antecedent endometritis, often of low grade.
15 to 25	<i>Broad ligament abscess.</i> Preceded by broad ligament cellulitis.

Puerperal pyelitis, or any other intercurrent infectious process, may appear at any time and bears no relation to the day of delivery.

As is usually the case with first editions, a few typographical errors are in evidence. These are of no particular importance except in one instance. On page 181, in describing the preparation of procaine solution, "fluidrams" should obviously read "fluidounces." The book should prove of great value to the busy general practitioner who wants to brush up on his obstetrics in a few hours of pleasant reading. The book should also serve as a handy reference manual of common facts, treat-

ments, and procedures. For this purpose the contents are well indexed and illustrated by photographs, line drawings, and charts. One may not always agree with the details of treatment outlined by Dr. Mengert, but more important to the reader is that the author backs up his treatment with facts and figures and impresses upon the reader the logic of the principles underlying his recommendations.

What Other Editors Think

CONSERVATIVE TREATMENT OF PERFORATED ULCER

FOR more than half a century the management of perforated peptic ulcer has epitomized all that is dramatic in modern surgery. The *mise-en-scène* is familiar to all: the patient lying in his agony in the receiving-room, his face pale and drawn, and his very speech hampered by the certainty of increasing his suffering; the surgeon calm and confident (for here is usually a diagnosis beyond doubt); and, in the background, the imminent presence of death.

The action moves to the theatre and then to the ward, where in a few days the patient, happy and comfortable and out of immediate danger, extols the skill of his surgeon. It is the surgeon's apotheosis. The fact that some of the very few patients who refuse operation recover and that some of the operated cases die has not seemed to detract from the general truth of this picture. Is this fantasy? When we try to ascertain the exact facts of the situation they appear to throw such doubts on its validity that some surgeons have recently abandoned the operative treatment of perforated ulcer in favor of conservatism. The evidence for such a revolutionary step will be weighed by all thoughtful surgeons, and their verdict will soon be forthcoming.

It is instructive to compare the theory of the conservative school with more orthodox opinion. Visick states that it is unnecessary to remove the peritoneal fluid and extravasated particulate matter: from this statement there will be little dissent. A great part of the fluid content of the peritoneal cavity is an exudate from the endothelial surface, which dilutes the irritating misplaced gastric contents. Gross particulate matter is rarely found, and indeed, as the perforation rarely exceeds a few millimeters in diameter, it is not to be expected. Few surgeons do more than aspirate the contents of Rutherford Morison's pouch and reserve drainage for the very late cases. Those who operate seek to close the perforation, believing that the perito-

neum can take care of itself if further soiling is prevented. The fact that perforated ulcers can close spontaneously has been known to observant surgeons for many years, but to argue from this that any given case is likely to do so is surely a logical error and may have dangerous implications.

At the present time the results of operative treatment in the best hands are so much better than those advanced by the advocates of conservatism that most surgeons will endorse Prof. Morley's opinion that non-operative treatment should be reserved only for the poor-risk cases. An improvement in the national mortality from this disease is more likely to result from earlier diagnosis and admission to hospital. One implication of great importance which emerges from this work is the use of gastric aspiration in cases of perforated ulcer if, for any reason, operation has to be deferred. If this alone is absorbed into routine surgical practice the protagonists of conservatism will have rendered a useful service.

British Medical Journal, No. 4485, p. 950.

DEATH UNDER ANESTHESIA

DEATHS during surgical operations do not seem to become any less common with advance in anesthetic technique. To a great extent this can be explained by the increasing boldness of surgery, where the dangers of the operation must be set against the certainty of early death from disease.

The dangerous emergencies of anesthesia are better prevented than treated—prevented, for example, by reasonable caution in the use of preoperative hypnotics and discretion in the use of thiopentone. There is, with the last, a band of laryngeal irritability between very light anesthesia, where stimuli may produce stridor but not the dangerous and persistent laryngeal spasm that is the usual cause of death, and relatively deep anesthesia, where the larynx is insensitive except to severe stimuli. When a potentially dangerous laryngeal

spasm does occur, the intravenous injection of as little as 5 mg. of *d*-tubocurarine chloride will relieve the situation; if this is not obtainable the anesthetist or surgeon should surely perform an emergency tracheotomy.

Heart-failure under anesthesia may conveniently be classified as primary and secondary. Primary cardiac failure applies to ventricular fibrillation and to cardiac asystole excited reflexly. Where fibrillation is present, the intracardiac injection of 10 ml. of 2 per cent procaine may restore a normal rhythm. Failing this, it may still not be too late for the heart to be stimulated into activity by cardiac massage after fibrillation has ceased from coronary anoxemia. The first need is to restore the cerebral circulation of oxygenated blood. The first stimulus to be applied, without delay, is auricular puncture through the third right intercostal space close to the border of the sternum, the needle being directed backwards and medially (the auricle is more sensitive than the ventricle to mechanical stimuli). If this fails, subdiaphragmatic cardiac massage should follow at once, though it is questionable whether "quick and forcible" movements may not sometimes do damage.

The very first step in resuscitation must be the establishment of a clear airway, including bronchial suction where this is appropriate, though preparation for cardiac massage need not wait on this.

With sufficient foresight in the early institution of intravenous fluid therapy, death from shock and hemorrhage in an operation can nearly always be prevented. The treatment of sudden hemorrhage should be the copious and rapid transfusion of blood. Where a cannula is already in a vein, the pressure from a sterile Higginson's syringe, which should be included in every transfusion outfit, will force blood through in spite of venospasm. If the apparatus is to hand, sternal puncture is more rapid and more certain. Though heart-failure in the operating-theatre will not be encountered often, so urgent is the need for effective treatment that, besides an *anesthetic emergency outfit* and tracheotomy instruments, blood-transfusion apparatus and a supply of plasma must be kept ready for immediate use.

During an operation the anesthetist's responsibility is seldom lighter than the surgeon's; with

minor operations it is heavier. Operative mortality will be reduced to a minimum only when every anesthetic is given or supervised by an experienced administrator who is also a good physician well versed in the practice of intravenous fluid therapy. The administrator will then be in charge of the patient, from his angle, from the time an anesthetic is decided on until the end of the immediate post-operative period. With the recognition that such a wide range of duties falls within the province of the anesthetist who has made himself competent to undertake them there will be no lack of recruits of suitable quality.

The Lancet. Vol. 253, p. 62.

CALORIE INTAKE AND INDUSTRIAL OUTPUT

THE publication *Science* has published a simple understandable report out of war-ridden Germany that teaches obvious nutritional lessons, especially the need of adequate protein in order to maintain weight when dietary fats have to be curtailed. There was an opportunity in Germany to appraise the unit output of workers in quite standardized employments, and to observe the effect of decreases or increases in terms of essential food trenchments or supplements. Whereas it was possible to add mineral and vitamin supplements, these were of no avail in the absence of basic foods and total calories consumed.

Thus, workers moving earth for an embankment or mining coal furnished the scientists with a chance to prove that "rationing of food also means a rationing of industrial production."

Coal miners in training were allotted 1,200 calories daily, out of a total of 2,800, for "work." They handled seven tons of coal daily or used up 170 calories per ton. The researchers advised adding 400 calories per day, and the output went up to nine tons daily at a unit expenditure of 155 calories. But at this level the workers averaged a weight loss of 1.2 kilograms in a period of six weeks, and, of course, that could not be long maintained. So they boosted the intake 800 calories, after which ten tons of coal were mined daily and the weights of the workers returned to normal.

It will immediately occur to many to ask about morale, living conditions, individual degrees of ambition or lethargy. For example, we are inclined to think that people living in temperate zones become tired and languid, like the natives, when they move to tropical climates. Against this evidence is the experience of Stillwell's engineers using weak and tired Chinese coolies and putting the famous road over the Hump. They were not capable of heavy work until they were fed more or less like football players, and then their accomplishment was prodigious. Commenting on what happened in Germany when food became scarce, the authors add, "Under existing conditions the job of one man often has to be done by two or three with a resultant higher total wage cost."

The amount of American production in peace and in war stems in great degree from well-fed workers. We have a munificent soil, a virile people, and to these has been added the power of the machine. Despite the sending of vast supplies of food (\$300,000,000 worth to our portion of occupied Germany alone, and a prospective three-fourths of a billion demand to carry them through 1948), we seem to have inspired envy far more than a desire to emulate our capitalistic motivated economy. The solemn facts of food should be pounded into the heads of politicians and peace planners. A world interchange of food and goods is needed far in advance of a dissemination of cockeyed ideas of rights, privileges, or ideologies.

E. L. Touhy, M.D., *Minnesota Medicine*, Vol. 30, p. 296; Carl B. Drake, M.D., Editor.

MEASURING RENAL FUNCTIONING

SEVERAL years ago Sodeman and Engelhardt devised a test for renal function which has many advantages over those commonly employed. The disadvantages of previous tests have been the discomfort to the patient because of a long period of

water restriction and the necessity of collecting the urine at various times during the period in which the test is going on.

Sodeman and Engelhardt found that if they gave posterior pituitary extract to their patients that the results are comparable to those in which the more elaborate procedures are carried out. The only procedure necessary is to give 0.5 cc. posterior pituitary extract subcutaneously and then collect the urine at one-half hour intervals for two hours.

A recent publication by Horne and Morris substantiates what Sodeman and Engelhardt observed in their original studies. The Bowman Gray School of Medicine observers furthermore found that the test in 25 patients who did not have kidney disease gave results comparable to the fluid restriction test. There was some difference in 27 patients with impaired kidney function but these changes were in no way of special significance because they were based upon the invalid assumption that one can expect the fluid restriction test always to give a constant result.

Horne and Morris noted that the pituitrin test accurately estimates the concentrating power of the kidney in patients with edema. Lastly, they concluded that the posterior pituitary test is of considerable value to the busy physician because it can be carried out in his office without any special preparation of the patient; it is finished within two hours and in the average patient causes no disturbing reaction. However, it should be borne in mind that pituitrin should not be given to the pregnant girl and potentially is dangerous to the patient who may have coronary arterial disease. The side effects of pituitrin, when given in doses of 10 U.S.P. units, are very slight. Occasionally the patient has abdominal cramps and in about 40 per cent they may have a painless stool. In none of the patients studied by Horne and Morris were there any significant changes in the blood pressure.

New Orleans Medical and Surgical Journal, Vol. 99, p. 469; John H. Musser, M.D., Editor in Chief.

New Drugs

The information in this department has been supplied to *Postgraduate Medicine* by the manufacturers of the products described.

DIHYDROERGOTAMINE "SANDOZ"

PURPOSE: For the relief of migraine headache.

COMPOSITION: Dihydroergotamine formed by the hydrogenation of the natural ergot alkaloid ergotamine.

DESCRIPTION: A specific for the relief of migraine headache, reported to be considerably less toxic than the natural alkaloid and having less tendency to produce undesirable side effects.

DOSAGE: 1 to 2 cc. subcutaneously, intravenously or intramuscularly. Repeat in one hour, if necessary.

CAUTIONS: There may be some reaction, such as nausea and vomiting, general malaise, and pain in legs. As used clinically, even in large doses, Dihydroergotamine "Sandoz" does not seem to alter the blood pressure but may slow the pulse rate.

HOW SUPPLIED: Ampules 1 cc. size in boxes of 6, 12, 50 and 100 ampules.

PRICE: D.H.E. 45—Dihydroergotamine "Sandoz"

Ampules, 1 cc.	Drug.	Phys.	List
Box of 6	2.40	2.65	4.00
Box of 12	4.14	4.55	6.90
Box of 50	15.25	16.90	...
Box of 100	29.40	32.60	...

PRODUCER: Sandoz Chemical Works, Inc., New York, N. Y.

PENICILLIN SODIUM, CRYSTALLINE, STERILE

PURPOSE: Penicillin therapy.

COMPOSITION: Each 25 cc. vial contains: 100,000 units or 200,000 units per vial.

DESCRIPTION: Crystalline penicillin sodium is thermostable and requires no refrigeration. Because of freedom from impurities it may be injected subcutaneously without causing discomfort.

INDICATIONS FOR USE: In the treatment of infections caused by penicillin-susceptible organisms.

DOSAGE: Subcutaneous, intravenous, or intramuscular injections of 20,000 units or more every three hours.

HOW SUPPLIED: 25 cc. vials containing 100,000 and 200,000 units.

PRODUCER: The Upjohn Company, Kalamazoo, Mich.

AMIGEN AND PROTOLYSATE

PURPOSE: To supply the amino acids essential for nutrition.

COMPOSITION:

Total nitrogen	12.0 per cent
Potential amino nitrogen	10.5 per cent
Amino nitrogen	7.8 per cent
Moisture	4.0 per cent
Ash	5.5 per cent

DESCRIPTION: Amigen is prepared from casein by pancreatic hydrolysis.

INDICATIONS FOR USE: *Oral* administration—used when whole protein is incompletely or unsatisfactorily utilized; when supplemental dietary protein is needed; for diagnostic purposes, and to buffer gastric acidity.

Parenteral administration—when the patient cannot or should not take food by mouth or cannot properly assimilate protein.

DOSAGE: From the standpoint of nitrogen, 1.3 gm. of Amigen is equal to 1 gm. of protein and when dosages are expressed as grams of protein they should be multiplied by 1.3 to convert to grams of Amigen.

CAUTIONS: In severe hepatic insufficiency, administration of Amigen should be approached with much caution. In liver insufficiency there may be inability to deaminate amino acids. Where intravenous fluids are contraindicated, as in congestive heart failure, solutions of Amigen should not be given.

HOW SUPPLIED: Amigen powder: 1-lb. cans, hermetically sealed, 12 to the case. Amigen 5 per cent in 5 per cent dextrose solution: 125, 500 and 1000 cc. flasks. 125 cc. flasks, 12 to the case; the two larger sizes, 6 to the case. Nutramigen consists of Amigen—20 per cent, olive oil—18 per cent; dextrose-maltose—42.3 per cent, starch—10 per cent, yeast—3 per cent, calcium gluconate—3.5 per cent and mineral salts—3.2 per cent. It is packed in 1-lb. cans, hermetically sealed under nitrogen, 12 to the case.

PROTOLYSATE, like Amigen, is an enzymic digest of casein, and consists predominantly of amino acids and polypeptides. Unlike Amigen, which may be employed both orally and parenterally, Protolysate is designed only for *oral* use.

PRODUCER: Mead Johnson & Co., Evansville, Ind.

PERFOLIN

PURPOSE: For nutritional failure of the aged, convalescence from infection or operation, pre-operative care, and prevention of deficiencies among sedentary workers, particularly in sunless northern climates.

COMPOSITION: Each capsule contains:

Vitamin A	25,000 U.S.P. units
Vitamin D	1,000 U.S.P. units
Thiamine (B ₁)	10 mg.
Riboflavin (B ₂)	5 mg.
Niacinamide	150 mg.
Ascorbic acid (C)	150 mg.
Folvite folic acid	5 mg.

DESCRIPTION: A new highly-potent multivitamin preparation which contains folic acid.

DOSEAGE: One or more capsules daily according to the needs of the patient, preferably as directed by a physician.

CAUTIONS: If prolonged therapy is indicated, these capsules should be taken under close medical supervision.

HOW SUPPLIED: Bottles of 100.

PRODUCER: Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

PLURAXIN

PURPOSE: Therapeutic formula for multiple vitamin deficiency.

COMPOSITION: A combination of vitamins A, B₁, B₂, B₆, C, and D with nicotinamide. Each capsule contains 25,000 U.S.P. units of vitamin A (from fish liver oil); 1000 U.S.P. units of crystalline vitamin D₂ (calciferol); 15 mg. of thiamine hydrochloride; 10 mg. of riboflavin; 2 mg. of pyridoxine hydrochloride; 150 mg. of ascorbic acid; 10 mg. of calcium pantothenate, and 150 mg. of nicotinamide.

INDICATIONS: Pluraxin is indicated for patients suffering from mild acute, mild chronic, and severe chronic multiple avitaminosis, when supplementary levels of vitamins do not, within a reasonable period of time, cause a reversal of the nutritional lesions.

DOSEAGE: Pluraxin is especially adapted to the dosage regimen recommended by the Council on Foods and Nutrition for the different vitamin deficiencies. The average therapeutic dose of Pluraxin is 2 capsules daily for one week or ten days. After this period, the administration of 1 capsule daily is sufficient.

HOW SUPPLIED: Boxes of 30 and 100 capsules.

PRODUCER: Winthrop Chemical Company, Inc., New York 13, N. Y.

PONTACAINE NEO-SYNEPHRINE

PURPOSE: Anesthetic and decongestive for topical use in the eye and nose.

COMPOSITION: Pontocaine Neo-Synephrine Aqueous Solution contains Pontocaine hydrochloride—0.25 per cent; Neo-Synephrine hydrochloride—0.25 per cent; boric acid—3 per cent; sodium bisulfite—0.1 per cent, and chlorobutanol (chloroform derivative)—0.4 per cent, are added as preservatives.

ACTION: Pontocaine hydrochloride exhibits a higher topical anesthetic efficiency than cocaine in corresponding concentration. Its conjoint use with Neo-Synephrine is particularly advantageous since the vasoconstriction exerted by the latter causes a prolongation of the analgesia and a decrease in toxicity.

INDICATIONS FOR USE: For temporary relief of pain and congestion in the eyes and nose which occur in the course of coryza, hay fever, conjunctivitis, flash burns and other injuries of the eye.

DOSEAGE: For ocular use 1 or 2 drops should be instilled into the lower conjunctival sac. For nasal use 2 drops are instilled into each nostril.

This may be repeated every three or four hours when necessary.

CAUTIONS: Use only according to the indicated directions. Pontocaine Neo-Synephrine Aqueous Solution should not be allowed to come in contact with metal; when applied by spray, only atomizers made of glass, hard rubber, or plastic parts should be used.

HOW SUPPLIED: Bottles of 1 fl. oz. and 8 fl. oz.

PRODUCER: Winthrop Chemical Company, Inc., New York 13, N. Y.

NITROLYSIN "RORER"

PURPOSE: Amino acid therapy

COMPOSITION: Contains natural enzymatic protein digest or hydrolysate derived from yeast and soya (including amino acids, B-complex vitamins, carbohydrate) approximately 60 per cent; added carbohydrate (largely sucrose) approximately 30 per cent; flavoring agents q.s.

DESCRIPTION: Provides a rich source of amino acids, with carbohydrate sufficient to ensure protein-sparing action, and added vitamins to correct vitamin deficiencies commonly occurring in hypoproteinemic states.

INDICATIONS FOR USE: In all hypoproteinemias for which oral amino acid therapy is indicated.

DOSEAGE: 1 tablespoonful, four or five times a day, or in larger doses, as directed by the physician. May be given in milk or water, or sprinkled on food.

HOW SUPPLIED: Plain or flavored, in bottles containing 250 gm.

PRODUCER: William H. Rorer, Inc., Philadelphia, Pa.

Correspondence

The letters in this month's Correspondence were written in comment on Dr. Wallace Marshall's discussion, "Whither the general practitioner?" which was published in the March issue of *Postgraduate Medicine*.

Communications from the readers of *Postgraduate Medicine* are always welcome and should be addressed to the Editors, 512 Essex Building, Minneapolis 2, Minn.

TO THE EDITOR:

I find Dr. Marshall's letter both interesting and stimulating; in many ways I agree with his conclusions.

My own feelings can be expressed simply. The ordinary citizen is on the lookout for the kind of doctor who gives the right sort of care to his patients because, as Dr. Francis Peabody said, "he cares so much for them." Education cannot manufacture this sort of product; it is a personal matter.

Nowadays, too many young doctors seem too little interested in the patient-to-physician relationship and are over-tempted by the lure of organized specialty practice which they see operate so successfully in the teaching hospitals. As Dr. Marshall points out, nobody has any quarrel with specialism; indeed, as scientific medicine grows, so, naturally, will specialism; on the whole, the best medical teaching, research and consultation services will be provided by those with special interests and skills. I fear, however, that the present popularity of specialism as a private venture depends in part, at least, upon a less altruistic hope which certain physicians cling to: that if they spend a sufficient length of time in postgraduate education after their medical school course, and pass a sufficient number of stringent examinations, they will at last receive a ticket which will entitle them to a larger income and greater prestige than non-ticket holders can obtain. This is unsound.

I wish that in our plan of education more emphasis could be laid on the dignity of our profession and that students could be taught to learn that the highest reward medicine has to offer to anyone is that of being known as a good doctor.

I wish recent graduates would realize that they all cannot be specialists. I wish more of them would hang out their shingles soon after their internships are completed, unafraid to start to work and unashamed to look after sick human beings tenderly, wisely and unselfishly as our great practitioners always have done.

I cannot agree so happily with Dr. Marshall's views about modern medical literature. I believe that doctors who happen to be interested in writing—and, on the whole, they are the ones who make the literature—do their best to express their ideas with clarity and brevity; this may be difficult because the nature of their subject matter may be so complex. I wish, however, that more doctors over the countryside would try to develop skill in the art of preparing papers. No carefully thought-out and critically put-together manuscript which adds to medical knowledge has difficulty in finding a vehicle for publication; an editor's trouble comes in obtaining material which meets these qualifications.

Yours sincerely,

REGINALD FITZ, M.D.

*Lecturer on History of Medicine and
Assistant to the Dean, Harvard
Medical School.*

TO THE EDITOR:

I have read Dr. Marshall's communication in the March issue with interest and I find myself in substantial agreement with him.

One of the most important problems before the medical profession of today is the problem of more adequate distribution of medical services and the keys to its solution are better distribution of physicians and better organization of medical services, particularly in rural areas and small communities. I hasten to add, however, that there is much to be done in the larger communities, too, where special-

ists tend to concentrate, in organizing their services on a voluntary basis in such a way that these services can be supplied more efficiently and at lower cost.

However, this is another problem and the one raised by Dr. Marshall is I think actually of greater importance. It is a complicated problem because general practitioners usually don't have access to the best hospital and laboratory facilities which are usually preempted by specialists. Needed are more community and rural hospital-health-laboratory-centers where the general practitioner can take his cases for diagnosis and when necessary for hospital care and for consultation with specialists.

I do not believe that there is very good prospect of solving the problem of the status and services of the general practitioner unless the medical schools create better attitudes on the part of medical students toward general practice. This is a difficult assignment because our medical faculties are made up almost entirely of specialists and the students are trained in hospitals where specialization of services is present to a high degree. This is inevitable, and indeed necessary, but I think that one healthy corrective would be for all students to have an opportunity to work for at least a short period under the supervision of carefully selected physicians in smaller communities and rural areas. Also during the regular hospital work as clinical clerks, greater emphasis should be placed on those procedures and laboratory tests which are available to any physician anywhere. There is unquestionably too great a concentration of interest and teach-

ing in most teaching hospitals on the bizarre, unusual, and complicated cases. This is important from the standpoint of diagnosis but many students lose perspective thereby unless there is some wise teacher on the staff who keeps the teaching emphasis in good balance.

I thoroughly agree with Dr. Marshall's attitude toward medical publications. I discovered as a general practitioner that I received little or no help from some of our medical publications partly because of lack of time to digest fully their excellent articles. Encouragement should be given to the widest distribution of publications which are designed for the benefit of the general practitioner.

The future status of the general practitioner is in my opinion the most important problem before the medical profession today and any method educationally, organizationally, and through publications which will develop greater pride of the general practitioner in his work, greater respect for general practitioners in the public's mind, and among professional organizations generally should be given every encouragement.

I have discussed this and related problems at considerable length in my recent monograph on "Medical Education and the Changing Order" published by the Commonwealth Fund in June, 1946.

Thank you again for giving me the opportunity to comment on Dr. Marshall's letter.

Sincerely yours,

RAYMOND B. ALLEN,

President, University of Washington.

CORRECTION

In the article, "Ideal Stumps and Prosthetics for Amputees," by Leonard T. Peterson, M. D., in the February issue of *Postgraduate Medicine*, the caption for Figures 1 and 2, p. 115 should read: Pylon for below-knee and above-knee stump as made in Prisoner of War Camps. On p. 116, the caption below Figure 3 should read: Prostheses for end-bearing thigh amputee (knee bearing) —should have stability on weight bearing, ease of control and durability.

After Office Hours

The "most-decorated" soldier is fifty-seven-year-old regular army Colonel Edgar Erskine Hume of the Medical Corps. At last count, he had 90 decorations—received from the United States and 36 other nations in the course of two world wars.

Colonel Hume is a descendant of six physicians of his name and line. His biography would fill a volume as large as this journal. He received his doctorate of medicine from the Johns Hopkins University in 1913. World War I made him a lieutenant colonel at 29, the youngest man to command a chain of field hospitals. During World War II, he was a temporary brigadier general.

As librarian of the Washington, D. C., Army Medical Library for a time between the two world wars, Colonel Hume sifted and read the voluminous incunabula, memoranda, notes, diaries, and other manuscripts housed there. These vast amounts of materials were later to be invaluable to him in the preparation of his various publications on literary, medical, and historical subjects.

His World War II Distinguished Service Medal was given for the sort of job he does best: stopping cold the Naples typhus epidemic in 1943.

Though proud of all his medals, Hume wears them only on official occasions. The most he ever wore at one time was in 1920 when he was received by the late King George V of England. That time he weighted down his tunic with four rows, eight to a row. Hume's greatest display these days is his six top U. S. ribbons and even that mod-



Official U. S. Army Photo

COLONEL HUME

esty jolts generals and GI's alike. Their jaws would drop even further if they realized that the Colonel had eighty-two more in his pocket.

* * *

A medical man should laugh at himself now and then to keep his spirits up, maybe even laugh at his colleagues—if he is willing to stand the risk.

We are reminded of a cartoon of two doctors talking in a hospital wardroom. One is saying: "Three months I've been treating him for jaundice and today he tells me he's a Chinaman."

Another cartoon depicts three men engaged in conversation in a crowded nightclub where a floor show is going on. One of the voluptuous, scantily-clad chorus girls, in a pout, whispers to another: "What the hell kind of men are they anyway—doctors or something?"

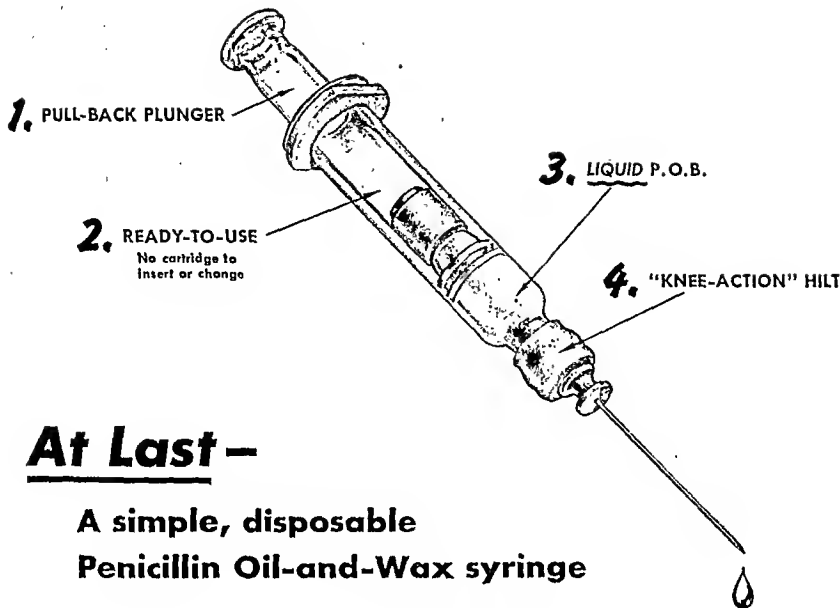
Now just one more: A row of black-robed sanctimonious professors are lined up before the commencement rostrum. A stalwart youth stepping up to receive his long-awaited and much prepared for M.D. is greeted thus: "Chase Medical School, University of — — — wishes you a long and honorable career—and may your first novel be a huge success."

* * *

Pain is the common phenomenon about which every doctor is forced, at one time or another, to speculate. Men build philosophies to explain and support it. It is, therefore, not idle dreaming to say that doctors who spend their time in efforts to fathom pain's sources should be able to write about it convincingly.

Samuel Johnson said: "A man should begin to write soon; for, if he waits till his judgment is matured, his inability, through want of practice, to express his conceptions, will make the disproportion so great between what he sees and what he can attain, that he will probably be discouraged from writing at all."

Doctor Axel Munthe, who in 1929 wrote *The Story of San Michele* or what is also sometimes called *The Memoirs of a Doctor*, tells us, "An old physician should think twice before sitting down in his armchair and writing his memoirs. Better keep to himself what he has seen of Life and Death. Better write no memoirs at all and leave the dead in peace and the living to their illusions."



At Last—

A simple, disposable Penicillin Oil-and-Wax syringe

1. PULL-BACK PLUNGER ... permits you to test for accidental puncture of a vein just as you always do. Simply pull back on the plunger. If no blood is aspirated—inject with confidence.
2. READY-TO-USE Cutter's Penicillin Oil-and-Wax syringe is ready to use "as is!"
3. NO HEATING This suspension at room temperature behaves like salad oil—rather than like butter. Easy to administer. (Cutter P.O.B. in vials also flows freely at room temperature!)
4. "KNEE-ACTION" HILT ... acts as shock absorber. Needle is mounted in rubber, allowing "play" without danger of snapping needle. After using, toss the entire syringe away.

NO NEED TO ACCEPT A SUBSTITUTE ... If these easy, ready-to-use Cutter syringes are not in stock, your pharmacist can get them...if you say the word.

Cutter Laboratories
Berkeley, California

CUTTER

Fine Biologics and
Pharmaceutical Specialties

However, he adds: "A man cannot live without sleep. When you cease to sleep then begin to write your memoirs, all milder remedies having failed." And that is just how Doctor Munthe happened to write *The Story of San Michele*—upon the advice of Henry James. Soon he slept better and no longer wondered why so many doctors were writing books.

Halliday Sutherland's *The Arches of the Years* published in 1933 is inevitably compared with Doctor Munthe's *The Story of San Michele* because they both relate stories of the doctors' patients and of extraordinary adventures that have nothing to do with doctoring. Doctor Sutherland's book tells of the life of a Scottish doctor. It is told with freshness, casualness and youthfulness, rather than with the disillusionment of age and experience.

* * *

A Philadelphia physician said he was doing some mighty interesting research on an aspect of clinical medicine and really should put his findings in a book—and before he could gracefully back out he actually had a publisher—but no manuscript. Worse, he felt he didn't have time to write it as it should be and besides the research was not finished. Now, if he wants to stay off the Best Seller list, this physician must quickly figure out some reason for NOT writing a book.

M. L. McD.

* * *

"OLD PEPYS" AT THE OPERA

During a Saturday afternoon broadcast of the Metropolitan Opera Company from New York, one of the questions used on the between-acts "Opera Quiz" was submitted by Old

Pepys of the Journal of the American Medical Association. If you'd like to see how well you would do as a medico-opera expert, here is a report of that portion of the Quiz:

Downes: Now for a question from the Editor of the Journal of the American Medical Association, Dr. Morris Fishbein. Dr. Fishbein advises that operas seem to include in their plots a goodly share of diseases and crimes. I think we have noticed this rather salient fact about operas.

Says Dr. Fishbein: There are six well-known musical deaths. Identify the opera and character involved in each.

1. *Asphyxia*:

Bagar: Old Rhadames in "Aida" in the last act is just asphyxiated.

Spaeth: Not only old Rhadames, but young Aida, too.

2. *Dementia*:

Bohm: Lucia, of course, in "Lucia di Lammermoor."

Downes: She's one of the prize dementia.

Bagar: Here's a real old one—Lothario in "Mignon."

3. *Traumatic Incision*:

Bagar: Practically any Italian opera—"Tosca," "Lucia"—self-inflicted, and otherwise, that is.

Downes: Now what is traumatic incision?

Bagar: Destruction with a cold blade.

Bohm: "Othello."

4. *Alopecia*:

Bagar: That's baldness.

Downes: Yes, and what opera?

Bagar: Osmin is bald—that is, when his wig is pulled off in the "Abduction from the Seraglio."

Downes: That has been so, at least on this stage.

Spaeth: And it had a lot to do with the death of Samson, both in "Samson and Delilah" and "The Warrior."

Downes: That's the answer that's given; he wasn't bald, but he certainly was shorn of his

hair, wasn't he?

Bohm: Close enough to lose his head.

Downes: We could say he was a victim of alopecia.

Bohm: Strictly speaking, that is not alopecia because alopecia is a congenital ailment.

Downes: Well, anyway, Dr. Fishbein nominates him. We will say that under the circumstances of his being an eminent scientist he is right.

5. *Cranial Trauma*:

Bohm: There is a great deal of that in all of Wagner. The "Tristan and Isolde" love potion, etc.

Downes: Now wait a minute, what is cranial trauma?

Bohm: An injury to the brain.

Downes: Well now, there's a place in the "Ring" that our correspondent suggests. What would you suggest.

Spaeth: That's the one where one giant slays the other one.

6. *Morsus Humanum*:

Bohm: What does that mean?

Downes: Well, if you must know it means a nip on the ear.

Downes: Two hands right away.

Bagar: Turridu in "Cavalleria Rusticana."

Spaeth: Well, I disagree a little about Turridu, because that was the insult which led to the duel, but he wasn't killed by that bite on the ear.

Downes: That's right, to be exact, that was the conventional form of challenge.

Contributions and suggestions for this department by readers of *Postgraduate Medicine* are always welcome. Address all communications to the Assistant Editor, *Postgraduate Medicine*, Essex Building, Minneapolis 2, Minn.

Notes on Contributors

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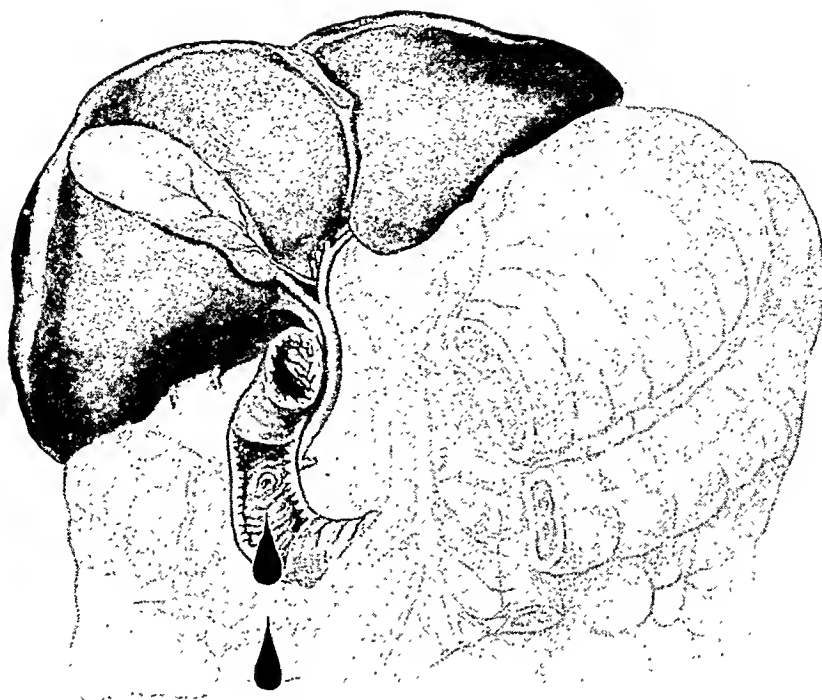
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*Albrecht, F. K.: Modern Management in Clinical Medicine. Baltimore, The Williams and Wilkins Co., 1946, p. 170.

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